2019 ANNUAL HIGHLIGHTS OF THE RESIDENT & FELLOW SECTION
NAVIGATING YOUR CAREER

Make this Experiential Learning Area your stop for comprehensive information on professional development at every career stage, including medical student, resident, fellow, junior faculty, senior faculty, and advanced practice provider. Look for the latest advice and information through a variety of interactive formats: one-on-one consults, 30-minute mentoring sessions, small group talks, and panel discussions.

Attend the Early Career Reception and Meet the Neurology Resident & Fellow Editorial Team

Monday, May 6 • 6:00 p.m.–9:00 p.m.
Grand Ballroom at the Philadelphia Marriott Downtown

Experience a unique place for undergraduate and graduate attendees to network with peers, find information about residency programs, on pursuing fellowships and/or careers in neurology academics, research, or practice, and get information about how the AAN can help support their careers.
### Residents & Fellows Editorial Team

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About the Cover: From the article: Teaching Video NeuImages: The signs of dystonic tremor: Tremulous “escanciador” by Jennifer Sharma, MD, Daniel Macias-Garcia, MD, Amir Zaidi, MD, and Alberto Espay, MD, MSc, Neurology September 18, 2018, 91 (12) e1204-e1205

Position of the arm required to elicit the hand tremor. Patient holds a bottle at the position that elicited her tremor (A; water bottle used as “hair curler”), reminiscent of the posture adopted by an escanciador, a Spanish cider cupbearer (B).


**Neurology Resident & Fellow Section**

**Section Editor**

**John J. Millichap, MD, FAAP**

John Millichap is a pediatric epileptologist in the Comprehensive Epilepsy Center, Ann & Robert H. Lurie Children's Hospital of Chicago, and assistant professor of neurology and pediatrics at Northwestern University Feinberg School of Medicine. Millichap completed his residency in pediatrics at the Brody School of Medicine and held fellowships in child neurology and clinical neurophysiology/pediatric epilepsy at Children's Memorial Hospital, Northwestern University. Millichap has over 35 peer-reviewed publications on pediatric neurology, epilepsy, and neuroinfectious disease. Current clinical practice utilizes a multidisciplinary team approach to the diagnosis and treatment of epilepsy and comorbidities. As a member of the academic faculty, he is involved in the education of trainees and grant-funded clinical research concerning epileptic encephalopathies. Millichap is an avid writer himself and enjoys encouraging resident and fellow contributions to the medical literature.

**Deputy Section Editor**

**Roy E. Strowd, MD**

Roy Strowd, assistant professor of neurology and oncology, is a neurologist and neuro-oncologist at the Wake Forest Baptist Medical Center. He graduated magna cum laude from Duke University in 2005 and from the Wake Forest School of Medicine in 2009. He completed residency in neurology at Wake Forest Baptist Medical Center in 2013, where he served as chief resident. He pursued fellowship training at Johns Hopkins, completing the clinical and research neuro-oncology fellowship program as well as dedicated training in medical education research through a fellowship supported by the American Academy of Neurology’s Medical Education Research Training Fellowship. Strowd has clinical research interests in drug development and response assessment in neuro-oncology as well as medical education interests in exploring optimal approaches for teaching health care professionals at multiple levels of training. Strowd is active in medical education, academic scholarship, and scientific research at both the local and national levels and truly enjoys each opportunity to mentor residents and fellows throughout neurology.

**Editorial Team, Resident & Fellow Section**

**Whitley Aamodt, MD, MPH**

Whitley Aamodt is an adult neurology resident at the University of Pennsylvania in Philadelphia. She graduated with a degree in neuroscience from the College of William and Mary and completed dual degrees in medicine and public health at the University of Texas School of Medicine at San Antonio. She is passionate about global and community health.

**Malik Muhammad Adil, MD**

Malik Adil is currently a vascular neurology fellow at NIH. He received his bachelor’s degree in medical technology from Jinnah Post Graduate Medical Center and medical degree from Shifa College of Medicine, Pakistan. Prior to neurology residency, he served as clinical research fellow at Zeenat Dureshi Stroke Center, University of Minnesota, where he engaged in research on stroke.

**Benjamin R. Claytor, MD**

Ben Claytor is an adult neurology resident at the University of Michigan. He graduated from Case Western Reserve University prior to obtaining his medical degree from the University of Illinois. His academic interests include neuromuscular medicine, medical education, and health care resource utilization.

**Guillermo Delgado-Garcia, MD**

Guillermo Delgado-Garcia is an adult neurology resident and a research assistant at the Instituto Nacional de Neurología y Neurocirugía in Mexico City. He received his medical degree from the Universidad Autonoma de Nuevo Leon (UANL), Mexico. After graduating medical school, he spent one year at the Instituto Nacional de Ciencias Médicas y Nutrición, Mexico, as a research assistant. He then completed residency in internal medicine at the University Hospital of the UANL.

**Ittai Bushlin, MD**

Ittai Bushlin is a child neurology fellow at Oregon Health and Science University. He completed a BA in brain and cognitive sciences at the University of Rochester before spending two years researching mechanisms of synaptic vesicle trafficking at NIH. He then attended Mount Sinai School of Medicine in New York City, where he obtained an MD and PhD. He completed his pediatric training at Oregon Health and Science University.

**Rachel Gottlieb-Smith, MD**

Rachel Gottlieb-Smith is a child neurologist at the University of Michigan. She graduated from Harvard College with a concentration in Biochemical Sciences and a secondary concentration in psychology. She received her MD from the Johns Hopkins University School of Medicine and completed her residency in child neurology at the Children’s Hospital of Philadelphia.

**Kwo Wei David Ho, MD, PhD**

David Ho is an adult neurology resident at the University of Florida in Gainesville. He graduated from the University of Virginia with degrees in chemistry and physics. He then went on to obtain his MD and PhD through the Medical Scientist Training Program (MSTP) at the University of Iowa.

**Emilio R. Garrido Sanabria, MD, PhD**

Emilio R. Garrido Sanabria is an adult neurology resident at Stony Brook University Hospital in New York. He received his medical degree from the Universidad de Ciencias Medicas de La Habana, Cuba, and obtained his PhD in neurosciences/neurology from the Universidade Federal de Sao Paulo, Brazil. He then completed post-doctoral training at Hadassah Medical Center, Jerusalem, and at the anatomy and neurobiology department, University of Maryland School of Medicine, before becoming a faculty member at the University of Texas at Brownsville where he directed an epilepsy research group.

**Robert Hurford, MSc, MRCP (UK)**

Robert Hurford is a neurology resident at Cambridge University Hospital, UK. He graduated in medicine from the University of Nottingham in 2011 followed by a master’s in clinical neuroscience at the Institute of Neurology, UCL. He has since pursued joint academic and clinical training, working with several stroke research groups, including in Manchester, Cambridge, and Paris.
Pouya Khankhanian, MD
Pouya Khankhanian is an epilepsy fellow at the University of Pennsylvania in Philadelphia, and a researcher at the Center for Neuroengineering and Therapeutics. He graduated with a degree in applied mathematics from the University of California at Berkeley before getting his medical degree at the University of California, San Francisco.

Regan Jo Lemley, MD, MS
Regan Lemley is a neurology resident at Wake Forest School of Medicine in Winston Salem, NC. She graduated from Southwestern University with a Bachelor of Science in biology and minor in philosophy. She then obtained a master’s in medical sciences prior to attending medical school at Texas Tech SOM. She will be an epilepsy fellow at Brigham and Women’s Hospital after completion of residency.

Ariel Maia Lyons-Warren, MD, PhD
Ariel Lyons-Warren is a child neurology resident at Baylor College of Medicine in Houston, Texas. She earned her Bachelor of Arts from Johns Hopkins University with a major in neuroscience and a minor in writing seminars. Prior to starting the medical scientist training program at Washington University in St. Louis, she spent six months working in a London theatre, backpacked across Europe, and then lived on a communal farm in Israel for six months.

Fábio Nascimento, MD
Fábio Nascimento is a neurology resident at Baylor College of Medicine. Originally from Brazil, he completed medical school at the Universidade Federal do Paraná (UFPR), and then spent two years at the University of Toronto working as a research fellow in epilepsy genetics. Subsequently, he moved to Houston, TX, to train as an adult neurologist.

Aaron Rothstein, MD
Aaron Rothstein is a neurology resident at the New York University School of Medicine. He graduated from Yale University in 2009 with a degree in history and from the Wake Forest School of Medicine in 2015. He writes regularly about medicine for The New Atlantis at http://practicing-medicine.thenewatlantis.com.

Behnam Sabayan, MD, PhD
Behnam Sabayan is an adult neurology resident at Northwestern Memorial Hospital, Northwestern University, Chicago. He has an established interest in brain aging and, in particular, the vascular contribution to brain structural and functional integrity. After medical school he received a Master of Science in aging and vitality and his PhD in clinical neuroscience from Leiden University in the Netherlands.

Jens Witsch, MD
Jens Witsch is an adult neurology resident at Yale University. He is originally from Freiburg, Germany, and studied medicine at the University of Heidelberg. He completed his neurology residency at the Chrátel in Berlin under the mentorship of Matthias Endres, Christoph Ploner, and Eric Jüttler, followed by a neurocritical care research fellowship in Jan Claassen’s group at Columbia University.

Alonso G. Zea Vera, MD
Alonso G. Zea Vera is a child neurology resident at Cincinnati Children’s Hospital Medical Center. He received his medical degree from the Universidad Peruana Cayetano Heredia, Peru. His research interests include neurophysiology, movement disorders, and cognitive neuroscience.
The *Neurology* Resident & Fellow Section

John J. Millichap, Roy Strowd, Kathleen Pieper

The *Neurology* Resident & Fellow Section (RFS) was founded in 2004 by Robert “Berch” Griggs, then the editor-in-chief of *Neurology*, and Karen Johnston, associate editor, who passed the reigns to Mitch Elkind several years later. By then, the “Page” had grown to a “Section,” with articles appearing weekly and a growing team of editorial members. The mission remained to keep our readers up to date on issues related to training and career considerations as well as support the development of lifelong learning skills. Currently, the RFS is trainee-run by an editorial team of more than 20 neurology residents and fellows with the responsibility for reviewing, editing, and publishing articles. Residents are selected annually through a competitive process that attracts dozens of applicants, and each will serve a three-year term. Past editorial team members have gone on to other important editorial activities, at *Neurology* and elsewhere, and they have found the experience a formative part of their careers. Dr. John Millichap, a former editorial team member and the current RFS Section Editor, assumed leadership of the section from Dr. Elkind in 2015. He is joined by Deputy Section Editor Roy Strowd, another former editorial team member. Photographs and brief biographies of the current Resident & Fellow Section editorial team can be found in this Highlights booklet.

The number of submissions to the RFS has increased dramatically (from 12 in 2004 to 773 in 2018), and the quality of published manuscripts has improved. Over the years, the RFS has also introduced several subsections which focus on (1) clinical neurologic education, such as Clinical Reasoning, Pearls & Oysters, Child Neurology, and Teaching Neuroimages; (2) graduate medical training, such as Journal Club, Global and Community Health, and Education Research; and (3) career issues, such as Emerging Subspecialties in Neurology and Mystery Cases that engage readers in interactive discussion of critical aspects of clinical neurology. Descriptions of these subsections appear in this Highlights booklet and include the top representative articles published in the past year as selected by the RFS editorial team members.

The RFS editorial team members have initiated and developed multiple unique projects, including podcasts (beginning in 2007), weekly E-Pearls (2008), an annual Writing Award (first given in 2009), and our website (launched in 2010). Our ongoing Call for Authors program, in which trainees throughout the world have the opportunity to sign up to write articles on selected topics, was launched in 2012. In 2012, we also began making all Teaching NeuroImages available as teaching slides. In 2014, members of the RFS editorial team were awarded the American Academy of Neurology Education Research Grant to study the role of mentored peer review of journal articles as a way of teaching evidence-based medicine and peer review skills to residents. The research project involved residents at nine US residency programs, and the results were presented at the AAN and other national meetings. In 2015, Luca Bartolini, editorial team member of the RFS, developed his original idea for “Practice Current: An interactive exchange on controversial topics” in collaboration with the editors of *Neurology*’s Clinical Practice (NCP). This has become a wildly popular section of NCP that aims to identify and discuss difficult clinical scenarios and diseases with conflicting or insufficient evidence regarding diagnosis or treatment. Other notable successful initiatives include the Clinical Reasoning book of previously published cases compiled to provide an educational resource for trainees and program directors, and the establishment of a RFS mentor-mentee pilot program designed to pair new RFS team members with recent graduates of the section. In years to come, we hope that this program may serve as a structured model for bringing new, young peer reviewers into the process, even outside the RFS itself.

The RFS webpage has exciting features such as rss feed for the expanded blog, special e-Pearls formatting, listings of the latest RFS articles, and online survey platform for the Mystery Cases. There are also links to other resident and fellow resources on the Neurology website and at AAN.com. We publish one RFS article in every print issue of *Neurology*, and there is a “Resident and Fellow Rounds” commentary written monthly by the RFS section editors that provides summaries of the RFS articles published with each issue. The RFS editorial team members are proud of the additional exposure through print distribution and expect that this will undoubtedly encourage the continued submission of high-quality manuscripts.

*Neurology* recognizes that the future of the journal, and the future of the field of neurology itself, depends on the interest and commitment of its readers and writers. This journal is one of the most important records of our profession, and current trainees are the profession’s most valuable resource. Accordingly, the RFS is strongly supported by *Neurology*’s current Editor-in-Chief Robert A. Gross, Executive Editor Patty Baskin, editorial staff, the AAN, and the publisher Wolters Kluwer. In particular, staff members Kathy Pieper and Robert Witherow have provided continual assistance and encouragement without which the section could not have survived. We welcome submission of manuscripts for the Resident & Fellow Section, and author instructions can be found at *Neurology*.org. Papers submitted for this section will undergo the same thorough peer review process as all *Neurology* submissions, and it is anticipated they will reflect the same high level of quality. It is further expected that manuscripts published in the section will carry the same academic weight, whether online or in print, as papers published elsewhere in *Neurology*. We also continue to welcome input from our readers, including program directors and other educators, on features that will be most valuable.

Questions and comments should be addressed to John Millichap, Roy Strowd, or Kathy Pieper at rfs@neurology.org. We hope you enjoy this year’s edition of the Highlights of the RFS!

John J. Millichap, MD, FAAN, Section Editor, Resident & Fellow Section
Roy E. Strowd, MD, Deputy Section Editor, Resident & Fellow Section
Kathleen M. Pieper, Senior Managing Editor
Top 10 Ways for Program Directors to Use the Neurology Resident & Fellow Section

John J. Millichap, Roy E. Strowd

Visit the Resident & Fellow Section (RFS) website at Neurology.org/residents_fellows to access the features below:

1. The “Clinical Reasoning” subsection presents clinical cases with valuable teaching points. The cases feature either unusual presentations of common diseases, or rare disease entities. The goal is to work through the case step-by-step, focusing on the patient presentation, exam, and diagnostic investigations. This subsection can be the basis for an educational conference, a morning report, or can be a great starting point for incoming residents to hone their neurologic skills. In addition, the RFS has published a book consisting of “Clinical Reasoning” highlights, available as a free download at the website.

2. The “Mystery Case” subsection features a case with an undisclosed diagnosis and asks readers a few multiple-choice questions to identify the relevant pathology; the case is also featured on our Facebook page. Residency programs are invited to incorporate these into their curricula and join in the friendly mystery case competition. Respondents can track their performance over time and compare their answers with others online.

3. Each “Teaching NeuroImage” has a supplemental PowerPoint slide set available for download from the Neurology website. These can be used for group presentations or for a rapid review of illustrative or unique imaging findings. Video submissions for “Teaching Video NeuroImage” are also welcome and have expanded the range of phenomena demonstrated in this subsection.

4. “Journal Club” articles provide critical appraisals of recent articles published in Neurology with a focus on research methodology. The format is ideal for guiding discussions at Journal Club meetings.

5. The “Emerging Subspecialties in Neurology” subsection offers valuable new ideas and viewpoints for residents considering different career options. The RFS website also provides a link to the AAN Fellowship Directory.

6. The “Global and Community Health” is a new subsection that welcomes manuscripts describing international neurology and care in resource-limited settings, home and abroad. Residents can describe international exchange programs. Students can review rotations abroad or volunteer opportunities in local resource-limited settings. This is a great opportunity to describe, review, and educate others on global and community neurology.

7. The Future of Neurology & Technology section focuses on the trainee perspective on neurology and technology. How is technology changing the way neurologists train and practice? What phone applications or devices are being used to enhance the neurologist’s clinical acumen, diagnostic accuracy, physical examination and patient interaction? For instance, was there a new phone application used to help patients track migraines? Was there a novel phone application used to help patients track their seizures? Was there an iPhone ophthalmoscope used to detect papilledema? How is this changing the practice of clinical neurology for students, residents, fellows, and neurologists? These articles provide a case-based discussion of new, emerging, or existing technologies that are being used with patients.

8. The “Education Research” subsection reports high-quality research on educational topics, including surveys of program directors and residents, as well as studies on educational interventions. Program directors and residents alike will enjoy the novel ways residents find to improve education in residency and beyond. These articles are also a helpful resource for rising chief residents who are exploring new approaches to resident education.

9. Many residents are interested in scholarly activities but may not know how to start. Program directors can help residents get involved by encouraging them to write for the RFS! Refer to the “Call for Authors” page on the website for ideas to jump-start the writing process. All published articles are considered for the Annual Resident & Fellow Writing Award.

10. Follow the RFS on Social Media: Join our Facebook group entitled “American Academy of Neurology Residents and Fellows” and check out our blog for new article publication announcements, and other information pertinent to neurology training. For further digital access to RFS content, listen to the weekly Neurology podcast, and follow Neurology Twitter for updates. Also, RFS is now posting on Instagram! Help spread the word!
Announcement

Neurology Resident & Fellow Section Writing Award

The Winners of the 2019 Award Are:

Nathaniel M. Schuster, MD, and Jacob R. Hascalovici, MD, PhD

For their article: Emerging Subspecialties in Neurology: Pain medicine

See page 26 of this Highlights book.

The Neurology Resident & Fellow Section Writing Award is intended to recognize the extraordinary writing abilities of those currently in training in neurology. Eligible manuscripts will include any submitted to and published in the Neurology Resident & Fellow Section, whether online or in print. Submissions on any topic of interest to trainees and in any subcategory of the section will be eligible. The main criteria for selection will be educational value, novelty, depth of exposition, and clarity of writing. At least one author of the manuscript must be a resident or fellow in one of the neurologic subspecialties. All authors will be considered equal recipients of the award in order to recognize and encourage collaborative work among trainees. The next award will be announced in early 2020 and will be awarded for a paper published in 2019.

No formal application process is required. All manuscripts submitted to the section will be considered. Manuscripts should be submitted online at NPub.org/submit. Please direct any questions to rfsection@neurology.org.

PAST RECIPIENTS

2018 Award Winner
For their article: Clinical Reasoning: An 82-year-old man with worsening gait
Sheena Chew, MD; Ivana Vodopivec, MD, PhD; and Aaron L. Berkowitz, MD, PhD
Neurology November 21, 2018, 89:21 e246-e252

2017 Award Winner
For their article: Episodic ataxia type 2: Case report and review of the literature
Elan L. Guterman, MD, Brian Yurgionas, MD, MS, and Alexandra B. Nelson, MD, PhD
Neurology June 7, 2016, 86:23 e239-e241

2016 Award Winner
Emerging Subspecialties in Neurology: Telestroke and teleneurology
Sunil A. Mutgi, MD; Alicia M. Zha, MD; and Reza Behrouz DO
Neurology June 2, 2015, 84:22 e191-e193

2015 Award Winner
Clinical Reasoning: An unusual cause of transverse myelitis?
Pavan Bhargava, MD, and Rodger J. Elble, MD, PhD
Neurology February 11, 2014, 82: e46-e50

2014 Award Winner
Right Brain: A reading specialist with alexia without agraphia: Teacher interrupted
Jason Cuomo, MA; Murray Flaster, MD, PhD; and José Biller, MD
Neurology January 7, 2014, 82:e5-e7

2013 Award Winner
Clinical Reasoning: A 55-year-old woman with vertigo: A dizzying conundrum
Daniel R. Gold, DO, and Stephen G. Reich, MD
Neurology October 23, 2012, 79:e146-e152

2012 Award Winner
Child Neurology: Brachial plexus birth injury: What every neurologist needs to know
Christina B. Pham, MD, Johannes R. Kratz, MD, Angélica Jelín, MD, and Amy Gelfand, MD
Neurology August 16, 2011, 77:695-697

2011 Award Winner
Right Brain: We were all once ‘fixed and dilated’
Amy Gelfand, MD
Neurology November 16, 2010, 75:1851
E-Pearls

May 2, 2018: Bobble-head doll syndrome

Bobble-head doll syndrome is a rare disorder characterized by repetitive head bobbing usually due to cystic lesions in and around third ventricle\(^1\). These movements may be due to: compression of the medial thalamus (which has somototopic motor representation of the head and neck); dilation of the third ventricle distorting dentatorubrothalamic pathways; or a learned behavior to open up the obstructed foramen of Monro\(^2\). Surgical decompression of the cyst results in clinical improvement.

References


Submitted by Sunil Munakomi, MCh, Neurosurgery — Kathmandu University, Nepal.
Dr. Munakomi reports no disclosures.

October 3, 2018: FOSMN syndrome

Facial onset sensory and motor neuronopathy (FOSMN) is a neurodegenerative disease that presents with paraesthesias and numbness in the trigeminal nerve distribution\(^1\). Within the first decade after its description, only 38 cases of FOSMN have been reported\(^2\). Data from this limited number of cases suggest the age of onset to be in the 6th decade and a higher prevalence in males\(^2\). Months to years after onset, patients typically develop lower motor neuron deficits progressing rostrocaudally\(^1,3\). Corneal reflexes are often absent. Neurophysiological studies typically show a sensory and motor neuronopathy\(^4\). Pathology shows a loss of sensory and motor neurons with TDP-43-positive inclusions\(^4\), putting FOSMN within the spectrum of motor neuron diseases. FOSMN is presumed to be sporadic and it is debatable whether it is a rare variant of amyotrophic lateral sclerosis.

References


Submitted by David Fam, MD, and Raphael Schneider, MD, Neuromuscular Fellows — Sunnybrook Hospital, University of Toronto.
Drs. Fam and Schneider report no disclosures.
Child Neurology

The Child Neurology section in the Resident & Fellow Section of *Neurology* focuses on contemporary educational issues in child neurology. The goal of the section is to provide up-to-date reviews on important topics in child neurology that are relevant to all neurologists, both adult and child, particularly those still in their training. Examples include management of acute stroke in children, childhood demyelinating disease, neuroimaging in metabolic disorders, and the neurobiology of autism. Each piece will begin with a patient case, followed by a brief discussion about the differential diagnosis and a detailed discussion about the topic of focus. Submissions are welcome from residents and fellows in either child or adult neurology. Ideally, submissions will include the patient case as well as the discussion, but submission of timely review articles without an accompanying case will also be considered. In this situation, the editors of this section may supply an appropriate patient case.
Child Neurology: Brown-Vialetto-Van Laere syndrome

Dramatic visual recovery after delayed riboflavin therapy

Ahmed K. Bamaga, MD,* Robi N. Maamari, MD,* Susan M. Culican, MD, Marwan Shinawi, MD, and Paul T. Golumbek, MD, PhD

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Brown-Vialetto-Van Laere syndrome (BVVL) is a rare, progressive neurodegenerative disease with fewer than 100 cases reported in the literature. It is characterized by pontobulbar palsy and sensorineural hearing loss.1 The age at onset varies from infancy to early adulthood, commonly presenting with cranial nerve VII–XII palsies and deafness. Other findings include gait ataxia, limb weakness, optic atrophy, epilepsy, and respiratory compromise.1 The genetic etiology of BVVL has recently been linked to mutations affecting the riboflavin transporter genes SLC52A2 and SLC52A3, which code for human riboflavin transporters RFVT2 and RFVT3, respectively.2 Consequently, several studies have reported improved clinical outcomes with riboflavin supplementation in patients confirmed to have mutations in the SLC52A2 and SLC52A3 genes.3–7 In this report, we describe a case of BVVL in a 6-year-old girl with dramatic visual recovery and neurologic improvement after delayed initiation of riboflavin supplementation. Consent was obtained from the child’s parents.

Case report

A 6-year-old girl was seen in the pediatric ophthalmology clinic after failing a vision screening test. Her family reported increasing clumsiness over the past year, resulting in frequent falls. On examination, her best-corrected visual acuity was 20/150 in each eye monocularly and 20/100 binocularly. She also was noted to have a small-angle exophoria with decreased stereopsis. The remainder of her ophthalmologic examination was unremarkable.

Visual evoked potential (VEP) testing demonstrated reduced amplitudes (∼60% of normal) and prolonged latencies (∼40 ms increased) on flash VEP and reduced acuity on spatial-sweep VEP testing. MRI of the patient’s brain and orbits revealed no intracranial abnormalities, but the optic nerves and tracts appeared mildly decreased in size. Based on these findings, the presumed diagnosis was bilateral optic nerve hypoplasia.

Approximately 13 months after initial presentation, the patient presented to the emergency department with progressive worsening in fine and gross motor skills. Physical examination demonstrated decreased visual acuity of 20/400 bilaterally and horizontal nystagmus in primary gaze that dampened with directional gaze. Sensory testing was normal and strength testing (table 1) was decreased for age with +1 tendon reflexes. She had bilateral dysmetria and prominent ataxia. She was born to healthy, nonconsanguineous parents without relevant family history, and had one healthy 4-year-old brother.

Laboratory testing included normal thyroid function testing, serum lactate and pyruvate ratio, and serum ammonia levels. Total plasma carnitine was slightly low for age at 34 μmol/L. Quantitative serum acylcarnitine profile was normal. Serum amino acid profile exhibited nonspecific abnormalities including mildly low glutamine and arginine levels and slightly

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elevated proline and α-amino butyric acid levels. CSF studies were normal with the exception of low homovanillic acid and 5-hydroxyindoleacetic acid. Chromosomal microarray was normal and genetic testing for Friedreich ataxia was negative.

EEG lacked a well-defined posterior dominant rhythm suggestive of mild generalized cerebral dysfunction. Nerve conduction and EMG showed small median compound muscle action potentials (CMAPs) but normal peroneal CMAPs. Sensory testing revealed absent median nerve action potentials from digit 2 and small for age sural nerve action potentials. These findings suggested a non-length-dependent axonal peripheral neuropathy or brachial plexopathy (table 2). The clinical presentation of optic atrophy, disproportionate upper extremity weakness, and ataxia, combined with the nerve conduction study findings suggesting an axonal peripheral neuropathy, raised suspicion for BVVL syndrome. Repeat MRI brain imaging did not demonstrate any change. Based on successful therapeutic interventions from previous reports, empiric treatment of 300 mg riboflavin (30 mg/kg) 3 times a day and coenzyme Q10 supplementation was initiated at that time, 16 months after the patient’s first presentation to the ophthalmologist with vision loss.1 When the patient demonstrated clinical improvement, riboflavin was increased to 500 mg (50 mg/kg/d) 3 times a day.

The clinical diagnosis of BVVL was subsequently confirmed by whole-exome sequencing, which identified compound heterozygous variants in SLC52A2. The first variant is paternally inherited and designated as c.245G>C:p.Arg82Pro. The second is a maternally inherited variant designated as c.1140delG:p.Leu381CysfsX9, which creates a frameshift starting with codon leucine 481 to cysteine, and results in a premature stop codon at position 9 of the new reading frame.

Ocular examination 18 months after initiation of riboflavin showed improvement in visual acuity to 20/20 bilaterally and complete resolution of nystagmus. Flash VEP testing demonstrated improved amplitudes (~82%, right eye; ~74%, left eye) and latencies in both eyes. Neurologic examination demonstrated improved coordination, gait, and muscle strength. Muscle strength measurements performed pre-treatment and after 12 months of riboflavin treatment are shown in table 1. A formal hearing study showed no impairment.

Of note, subsequent targeted genetic testing also confirmed the same compound heterozygous variants in the patient’s 4-year-old brother who exhibited mild symptoms including tremor when holding heavy objects and occasional choking episodes. At 2 years of age, he was found to have a significant hyperoparetic refractive error (~7.0 diopters) causing a 30-diopter refractive esotropia and strabismic amblyopia in the left eye. Prescription glasses improved the esotropia, and he began atropine penalization treatment for amblyopia. A preferential look test performed at age 3 showed mild residual amblyopia of the left eye, and he was switched to patching therapy for treatment of amblyopia. After a thorough discussion with the family regarding the progressive nature of BVVL, the younger sibling was initiated on 200 mg (30 mg/kg/d) of riboflavin taken 3 times daily and 100 mg of CoQ10 taken twice daily. He has remained asymptomatic. At his last assessment at age 6, his minor neurologic abnormalities had resolved and no additional findings had appeared. His hearing remained normal and his ophthalmologic findings were stable, with flash VEP testing showing mild reduction of amplitude suggestive of early, asymptomatic BVVL syndrome.

### Table 1 Quantitative muscle strength test results demonstrating muscle strength in pounds before and after treatment with riboflavin

<table>
<thead>
<tr>
<th>Muscle</th>
<th>Before treatment (right side/ left sides)</th>
<th>After treatment (12 mo) (right side/ left sides)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder abduction</td>
<td>6/8†</td>
<td>10/11</td>
</tr>
<tr>
<td>Arm flexion</td>
<td>3/3†</td>
<td>7/7†</td>
</tr>
<tr>
<td>Arm extension</td>
<td>10/12†</td>
<td>15/15†</td>
</tr>
<tr>
<td>Wrist extension</td>
<td>0/0.5†</td>
<td>1/2†</td>
</tr>
<tr>
<td>Hip flexion</td>
<td>20/20†</td>
<td>32/34</td>
</tr>
<tr>
<td>Knee extension</td>
<td>20/21†</td>
<td>34/32</td>
</tr>
<tr>
<td>Knee flexion</td>
<td>19/22†</td>
<td>25/26</td>
</tr>
<tr>
<td>Foot dorsiflexion</td>
<td>18/18†</td>
<td>27/31</td>
</tr>
</tbody>
</table>

*Values that are low for age based on clinical experience (P.T.G.).

## Discussion

BVVL syndrome is a treatable genetic condition caused by mutations affecting the genes that code for riboflavin transporters. Riboflavin is absorbed in the small intestine by human riboflavin transporters RFVT1 and RFVT3, and is exchanged in the brain via a third transporter, RFVT2. Riboflavin is the precursor for essential flavo-coenzymes ([flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD)])). FMN and FAD are important coenzymes that catalyze the various electron transfer reactions involved in fatty acid
Table 2  Nerve conduction and EMG study results showing evidence of non-length-dependent axonal neuropathy

<table>
<thead>
<tr>
<th>Nerve/sites</th>
<th>Latency, ms</th>
<th>Amplitude, mV</th>
<th>Segments</th>
<th>Distance, mm</th>
<th>Latency diff</th>
<th>Velocity, m/s</th>
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</thead>
<tbody>
<tr>
<td><strong>MNC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R median—APB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrist</td>
<td>4.69</td>
<td>0.8</td>
<td>Wrist—APB</td>
<td>70</td>
<td></td>
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<tr>
<td>Elbow</td>
<td>7.97</td>
<td>0.7</td>
<td>Elbow—wrist</td>
<td>148</td>
<td>3.28</td>
<td>45.1</td>
</tr>
<tr>
<td>R peroneal—EDB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ankle</td>
<td>4.58</td>
<td>4.4</td>
<td>Ankle—EDB</td>
<td>100</td>
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<td></td>
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<tr>
<td>Fib head</td>
<td>9.22</td>
<td>6.3</td>
<td>Fib head—ankle</td>
<td>223</td>
<td>4.64</td>
<td>48.1</td>
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<tr>
<td>Pop fossa—ankle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>SNC</strong></td>
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<td></td>
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<tr>
<td>L median, ulnar—digits 2, 4, 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median digit 2</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>140</td>
<td>NR</td>
</tr>
<tr>
<td>R sural—ankle (calf)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calf</td>
<td>2.8</td>
<td>3.4</td>
<td>6</td>
<td>2.8</td>
<td>140</td>
<td>51</td>
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</tbody>
</table>

**EMG**

<table>
<thead>
<tr>
<th>Summary</th>
<th>Insertional activity</th>
<th>Spontaneous</th>
<th>MUAP</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>L deltoid (middle)</td>
<td>Normal</td>
<td>None</td>
<td>None</td>
<td>Sl Incr</td>
</tr>
<tr>
<td>L fist dorsal interosseous</td>
<td>Normal</td>
<td>2+</td>
<td>2+</td>
<td>None</td>
</tr>
</tbody>
</table>

Abbreviations: Amp = amplitude; APB = abductor pollicis brevis; Cond vel = conduction velocity; EDB = extensor digitorum brevis; Fasc = fasciculation; Fib = fibrillation; lat = latency; MNC = motor nerve conduction; MUAP = motor unit action potential; NR = no response; PSW = positive sharp wave; Sl Incr = slight increase; SNC = sensory nerve conduction.

oxidation. Interestingly, recent work has identified mutations in the genes SLC52A2 (coding for RFVT2) and SLC52A3 (coding for RFVT3) as the cause of many cases of BVVL syndrome. As a result of this discovery, treatment with high-dose riboflavin supplementation has significantly improved morbidity and mortality rates in a condition that was previously often fatal due to respiratory failure. Furthermore, Foley et al. demonstrated an increase in riboflavin levels in 9 out of the 10 patients assessed before and after initiation of riboflavin therapy.

A review of the literature revealed 47 cases where riboflavin treatment was initiated; however, only 38 reports documented the clinical treatment response (24 RFVT2 cases; 14 RFVT3 cases). Clinical improvement was reported in 28 patients (74%) and stabilization without progression was documented in the remaining 10 patients (26%).

In regards to the effect of riboflavin treatment on optic atrophy, only 3 of the 17 cases with optic atrophy provided documentation on specific visual function change after treatment. A previously reported case of a 2-year-old girl with the SLC52A2 mutation showed visual acuity improvement to 20/300 after 6 months of riboflavin treatment. Mild visual improvement after initiating treatment was also seen in 2 patients with SLC52A2 mutations (11-year-old girl; 2-year-old boy). In this report, we describe a 6-year-old girl who exhibited remarkable visual recovery from 20/400 to 20/20, as well as improvement on VEP studies. To our knowledge, this could be one of the most dramatic recoveries in visual function reported after treatment with riboflavin.

The magnitude of visual recovery raises many questions regarding the downstream cellular effect of the SLC52A2 and SLC52A3 mutations. Variable neurohistopathologic findings of neuronal loss, myelinated fiber loss, and gliosis in the brainstem cranial nerve nuclei and anterior horns of the spinal cord with accompanying nerve root atrophy were reported in 2 patients with genetically confirmed SLC52A2 gene mutations who were not treated with supplemental riboflavin. Given the magnitude of visual improvement exhibited in the present case, the mutation in BVVL syndrome likely does not...
result in an isolated axonal loss. We hypothesize a combined axonal neuropathy with coinciding reactive demyelination as a result of microglia and macrophage infiltration. However, initiation of riboflavin supplementation may halt further axonal death and reduce additional microglia- and macrophage-induced inflammation. Consequently, areas with myelin loss may undergo remyelination, producing a recovery in neuronal function as exhibited in our patient.

It is critical to consider BVVL syndrome in the differential diagnosis in patients presenting with cranial neuropathies, balance difficulties, and sensorineural hearing loss. Treatment with riboflavin supplementation should be initiated immediately while awaiting genetic confirmation. In addition, extensive genetic counseling should be provided to affected families, and genetic screening for at-risk family members should be recommended to identify any asymptomatic siblings with positive molecular results who may benefit from prophylactic riboflavin treatment.

**Author contributions**

A.K. Bamaga: data collection, literature review, writing the manuscript. R.N. Maamari: data collection, literature review, writing the manuscript. S.M. Culican: data interpretation, critical revision of the manuscript. M. Shinawi: data interpretation, critical revision of the manuscript. P.T. Golumbek, data interpretation, critical revision of the manuscript.

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**References**


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Clinical Reasoning

Clinical Reasoning focuses on case presentations with the aim of developing clinical reasoning skills among trainees. Appropriate cases for publication would include uncommon presentations of common neurological disorders and also typical presentations of more exotic disorders. The emphasis of the case presentation should be on generating a sound, thorough differential diagnosis; logically arriving at the correct diagnosis; and thoughtfully discussing the teaching-points of the case. Cases discussed in the section should utilize data presented serially in two to four segments that could be opened sequentially by the reader, allowing them to challenge themselves by thinking through the differential diagnosis or treatment options at each step. The manuscript should indicate where each break would occur, with specific questions for the reader to consider as they work their way through the case. The final section should provide the experienced clinician’s discussion (or resident author’s literature review). Ideally the individual sections will also include visually presented data, such as radiology, EEG, EMG, or other studies. See published samples as examples.
Clinical Reasoning: A 23-year-old woman with fever and vertical diplopia

David J. Lin, MD, Seth N. Levin, MD, Catherine S.W. Albin, MD, Anna E. Goodheart, MD, and Nagagopal Venna, MD


Section 1

A 23-year-old woman with a history of uncomplicated migraine headaches presented with 2 days of headache. Her typical migraines were preceded by visual aura and usually resolved after taking a triptan. This headache was different in that there was no preceding aura, it did not respond to Imitrex, and it was accompanied by nausea/vomiting, dizziness, subjective fevers, and binocular vertical diplopia. She had had a mild upper respiratory tract infection 1 week prior to presentation. She had no sick contacts or recent travel history. Initial bedside examination showed hypertropia OD (figure 1) that did not change with direction of gaze. The degree of hypertropia improved with supine positioning. Her extraocular movements were otherwise not restricted, and her pupillary responses were normal. She had no other abnormalities on her neurologic examination.

Questions for consideration:
1. How would you describe the ocular abnormality?
2. What is the expected localization?
3. What is the differential diagnosis?

Figure 1 Skew deviation

A 23-year-old woman presented with vertical diplopia and was found to have a hypertropia OD consistent with skew deviation.
Section 2

Our patient's vertical diplopia, which occurred in all positions of gaze and improved with supine positioning, was most consistent with skew deviation. Skew deviation is a vertical misalignment of the eyes that results from a supranuclear disruption of conjugate vertical eye movements. It results from damage to the vestibulo-ocular system, which normally maintains eye fixation during head movements.

The otoliths (saccules and utricles) and semicircular canals detect linear and angular acceleration, respectively, coordinating vertical eye movement in response to head position. Projections from the utricle and semicircular canals synapse on vestibular nuclei. Second order fibers cross the midline, ascend via the medial longitudinal fasciculus (MLF), and innervate the third and fourth cranial nerve nuclei, the rostral interstitial nucleus of the MLF, and interstitial nucleus of Cajal. The latter nuclei reside in the midbrain and coordinate vertical gaze. An injury to any part of this pathway, spanning the peripheral nervous system and CNS, can cause skew deviation. Lesions in different locations classically result in types of skew as delineated by careful clinical observation. For example, lesions of the utricle result in upward deviation of both eyes with different amplitudes; lesions in the drowsolateral medulla result in hypertropia of one eye with the other eye remaining in the primary position; and lesions in the midbrain tegmentum result in simultaneous hypertropia of one eye and hypotropia of the other eye.\(^1\)

The combination of head tilt, ocular torsion, and skew deviation is known as the ocular tilt reaction. Head tilt is a maneuver to compensate for a shifted vertical meridian. For example, a lesion in the left utricle causes the brain to perceive that the head is tilting to the right. The head rotates in the counterclockwise direction (leftward) to compensate. Lesions in the utricle, caudal brainstem, or cerebellum usually result in ipsilateral head tilts, while lesions rostral to the midpons result in contralateral head tilt.

Ocular torsion or cyclotorsion describes rotation about the visual axis of the eyes and results from aberrant nuclear control of extraocular muscles. Third nerve subnuclei normally control ipsilateral inferior rectus and inferior oblique muscles. The third nerve superior rectus subnucleus and trochlear nucleus control the contralateral superior rectus and superior oblique muscles, respectively. As a result, injury along the MLF will cause the ipsilateral eye to appear hypertropic (inferior rectus palsy) and incyclotorted (inferior oblique palsy), and the contralateral eye to appear hypotropic (superior rectus palsy) and excyclotorted (superior oblique palsy). Notably, if the lesion causing skew occurs before the vestibular-ocular projections cross the midline and join the MLF (i.e., in the vestibular apparatus or pontomedullary junction), the ipsilateral eye will be hypotropic and excyclotorted, and the contralateral eye will be hypertropic and incyclotorted.\(^2\)

The hypertropia of skew deviation is generally the same in all positions of gaze, i.e., comitant, which usually differentiates it from a fourth nerve palsy. However, this is not always the case as there can be incomitant skew deviations. Another distinguishing maneuver between skew deviation and trochlear nerve palsy is the upright-supine test. The vertical misalignment of a skew deviation should decrease by at least 50% when the patient moves from an upright to supine position.\(^3\) This likely results from a shift in the utricular axis during the transition from supine to upright. Since utriculo-vestibular pathways are not affected by infranuclear lesions, the same change in vertical misalignment with change in position should not be seen with a fourth nerve palsy.

Our patient's skew deviation accompanied by nausea and vomiting best localized to the caudal part of the floor of the fourth ventricle along the area postrema. She did not have a clear head tilt and cyclotorsion was difficult to detect on bedside testing, but the comitant hypertropia with positive upright-supine testing pointed away from a fourth nerve palsy, and allowed us to diagnose skew and localize supranuclearly.

The differential for the patient's clinical presentation was broad and included vascular, neoplastic, inflammatory, and infectious processes. A brainstem stroke could cause skew deviation, but would be unlikely in this previously healthy young woman with no vascular risk factors. Posterior fossa tumors, in particular ependymoma, can present with isolated brainstem signs. In a young woman, demyelinating conditions such as multiple sclerosis and neuromyelitis optica require consideration. Given her history of subjective fevers and the recent upper respiratory tract infection, inflammatory and infectious etiologies with a predilection for the brainstem such as listeria, mycoplasma, tuberculosis, fungal infections, and atypical viral infections (i.e., varicella-zoster virus [VZV], herpes simplex virus [HSV], and West Nile virus) were at the top of our differential diagnosis.

**Question for consideration:**

1. What further diagnostic tests would be helpful?
Table 1. CSF profile at 2 different time points during hospitalization

<table>
<thead>
<tr>
<th></th>
<th>Hospital day 1</th>
<th>Hospital day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cell count</strong></td>
<td>20 (70% neutrophils)</td>
<td>200 (75% lymphocytes)</td>
</tr>
<tr>
<td><strong>Glucose</strong></td>
<td>73</td>
<td>55</td>
</tr>
<tr>
<td><strong>Protein</strong></td>
<td>44</td>
<td>67</td>
</tr>
</tbody>
</table>

Section 3

Initial brain MRI showed no specific abnormalities to explain the patient’s symptoms or examination findings. On hospital day 1, she spiked fevers to 103°F. Her CSF was notable for a neutrophilic pleocytosis with normal protein and glucose (table).

On hospital day 3, the patient developed new flaccid right arm weakness. A repeat brain MRI revealed diffuse T2 hyperintensities, which involved the floor of the 4th ventricle. Spine MRI showed longitudinally extensive T2 hyperintensities along the anterior horn of the cervical cord (figure 2). This anterior cord lesion likely explained her arm weakness.

A repeat lumbar puncture on hospital day 4 showed an increased pleocytosis with a shift from a neutrophilic to lymphocytic predominance and elevated protein (table).

A broad infectious workup was notable for a positive serum *Mycoplasma pneumoniae* immunoglobulin M (IgM) with a positive confirmatory immunofluorescence. CSF PCR for mycoplasma was negative. Negative infectious workup included negative bacterial and fungal cultures as well as negative dedicated testing for HSV, VZV, Epstein-Barr virus, HIV, echovirus, syphilis, Lyme, Cryptococcus, West Nile virus, enterovirus, and Chikungunya virus. Autoimmune testing including serum and CSF neuromyelitis optica antibodies were negative.

Questions for consideration:
1. What is the final diagnosis?
2. How would you treat this patient?

Figure 2. Brain and spine MRI

(A) Axial T2 fluid-attenuated inversion recovery brain MRI reveals T2 confluent hyperintensity in the dorsal pons and surrounding the 4th ventricle. (B) Sagittal T2 STIR cervical spine MRI shows linear T2 hyperintensity spanning the length of the anterior portion of the cervical cord. (C) T2 axial spine MRI at the level of the C2 shows T2 hyperintensity forming an outline of the anterior horn cells and gray matter structures.
Section 4

With the positive serum *M. pneumoniae* IgM and confirmatory immunofluorescence test, we diagnosed the patient with mycoplasma encephalomyelitis.

The patient received a 5-day course of azithromycin beginning hospital day 3 (empiric treatment initially, which continued when serum serologies for mycoplasma returned positive). Given the lack of mycoplasma DNA in her CSF, the timing of her neurologic symptoms, and a positive IgM serology for *M. pneumoniae*, we suspected a primarily immune-mediated parainfectious pathophysiology. Consequently, she also received a 5-day course of IV immunoglobulin (IVig).

The patient’s symptoms rapidly improved with treatment. By the time of discharge (hospital day 9), her vertical diplopia was stable and her right arm strength improved such that she could lift the arm antigravity without difficulty.

At 3-month follow-up, the patient had no diplopia, a subtle right hyperphoria, and only subtle residual right arm weakness. She noticed difficulty fully opening the left side of her jaw—she was unable to open her mouth wide enough to eat hamburgers. Examination revealed wasting of the left masseter muscle and deviation of her jaw to the left. Review of her in-hospital MRI showed T2 hyperintensity in the area of the motor nucleus of cranial nerve V in the pons, which accounted for difficulty with mastication (figure 3).

Discussion

*M. pneumoniae* has been associated with a diverse range of neuropathologies that can affect any location in the neuraxis including central (encephalitis, acute disseminated encephalomyelitis, transverse myelitis, striatal necrosis, aseptic meningitis, opsoconus-myoclonus, optic neuritis, strokes, and seizures) as well as peripheral (Guillain-Barré syndrome, polyradiculitis, and cranial nerve palsies). Encephalitis, a common manifestation, is more frequently reported in children than adults.4 CNS demyelination is a frequent pathologic endpoint in mycoplasma infections, which can cause a life-threatening acute disseminated encephalomyelitis. Demyelination may also affect the spine alone, presenting as transverse myelitis. In addition to skew deviation, ocular presentations of *M. pneumoniae* include opsoconus-myoclonus, optic neuritis, and neuroretinitis. *M. pneumoniae* has a predilection for the brainstem and has been implicated in cranial nerve palsies as well as Bickerstaff brainstem encephalitis.

Several possible mechanisms may account for the wide variety of neurologic manifestations associated with *M. pneumoniae*. Some studies propose direct bacterial invasion of the CNS, while others postulate an immune-mediated, parainfectious effect, citing autoantibody production as the primary mode of injury. Alternatively, immune complex deposition may cause CNS vasculitis and tissue ischemia.

Given the lack of mycoplasma DNA in our patient’s CSF and the timing of her neurologic symptoms, we suspected an immune-mediated, parainfectious pathogenesis. Indeed, *M. pneumoniae* is often not detected in CSF in cases of mycoplasma encephalitis; one study estimates that DNA is only detected in CSF in up to 14% of cases. A neutrophil-dominant vs lymphocyte-dominant pleocytosis has also been postulated to indicate direct bacterial invasion vs parainfectious immune-mediated mechanisms. In our case, we observed an increasing pleocytosis between hospital day 1 and day 4 with a shift from neutrophil-dominant to lymphocyte-dominant CSF. This shift potentially favors a parainfectious mechanism, but this is currently speculative.

No randomized trials exist to guide management of the neurologic complications of *M. pneumoniae* infection. Antibiotics and immunomodulating therapy are considered the cornerstones of therapy. It is unknown if early treatment with antibiotics can prevent neurologic sequelae. However, since the bacterium itself may be responsible for CNS damage, antibiotic treatment is recommended. Immunomodulating therapies have been implemented with varying degrees of treatment success. Case reports highlight a role for
corticosteroids. Plasma exchange has also been tried, but usually in cases of IVIg treatment failure.

Our case highlights the utility of IVIg in modulating the suspected immune-mediated injury in patients with *M pneumoniae*-related neurologic injury. Rationale for the use of immunoglobulin derives from nonspecific inhibition of multiple inflammatory pathways. In our case, early initiation of IVIg was associated with rapid improvement of symptoms. Prior case reports have also documented swift recovery and long-term resolution of neurologic symptoms after treatment with IVIg. This report adds to the growing body of cases supporting a role for IVIg in shortening the duration and severity of *M pneumoniae* parainfectious neurologic complications.

**Author contributions**

David J. Lin: manuscript concept, drafting, revision. Seth N. Levin: manuscript drafting and revision. Catherine S.W. Albin: manuscript drafting and revision. Anna E. Goodheart: manuscript drafting and revision. Nagagopal Venna: critical revision of manuscript for intellectual content.

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**Disclosure**

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**References**

Education Research

As the central mission of *Neurology*, education is a top priority. This is a section for interventional educational studies, as well as more traditional educational research, such as surveys. This section will examine the way neurologists not only practice, but also the way we teach and approach education. Neurologists have traditionally been respected, perhaps above all other specialties, for their scholarship and teaching. Educational issues will therefore continue to be at the center of the mission of *Neurology*.
Education Research: Physician identification and patient satisfaction on an academic neurology inpatient service

Christopher R. Leon Guerrero, MD, Tracy Anderson, BS, and Allyson R. Zazulia, MD

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Abstract

Objective
To determine the relationship between neurology inpatient satisfaction and (1) number of physicians involved in the patient’s care and (2) patients’ ability to identify their physicians.

Methods
A 10-item questionnaire addressing patient satisfaction and identification of physicians on the care team was administered to patients admitted to an academic, tertiary care, inpatient neurology service from May 1 to October 31, 2012. We hypothesized higher satisfaction among patients having fewer physicians on the care team and among patients able to identify their physicians.

Results
A total of 652 patients were enrolled. An average of 3.9 (range 3–8) physicians were involved in each patient’s care. Patients were able to correctly identify on average 2.4 (60.7%) physicians involved in their care. Patients who were very satisfied correctly identified a larger percentage of physicians involved in their care (63.8% vs 50.7%, p < 0.001), were more likely to identify a physician who knew them best (94.3% vs 43.6%, p < 0.001) and who was “in charge” of their care (94.1% vs 57.6%, p < 0.001), and were more likely to have private insurance (82.8% vs 70.5%, p < 0.001) and fewer physicians involved in their care (3.84 vs 4.06, p = 0.02).

Conclusions
Neurology inpatients’ ability to identify physicians involved in their care is associated with patient satisfaction. Strategies to enhance patient satisfaction might target improving physician identification, reducing actual or perceived disparities in care based on payer status, and reducing handoffs or conducting handoffs at the bedside.
A challenge of academic neurology inpatient services is that the physician team caring for each patient typically involves numerous providers and trainees. In addition, restructuring of training programs to meet increasing duty hour restrictions over the last decade have resulted in a shift work model, leading to even more providers involved in a patient’s care. With the current system of coverage, it is conceivable for a patient to be cared for by as many as 5 to 10 physicians even during a brief hospitalization. Prior evidence suggests that patients’ satisfaction is influenced by their ability to form a personal relationship with their physician and is thus affected by their ability to identify their physicians and the physicians’ role in their care. However, patients treated in an academic setting often cannot identify who their physicians are or their level of training.

In this study, we sought to determine physician-related factors that may influence patient satisfaction on an inpatient academic neurology service as well as the relationship between patient satisfaction and physician identification. We hypothesized that (1) patients are more likely to be satisfied with their care when fewer physicians are involved in their care and (2) a patient’s ability to identify the physicians involved in his or her care is associated with greater patient satisfaction.

Methods

We conducted a prospective survey of consecutive patients admitted to the adult neurology inpatient service at Barnes-Jewish Hospital (BJH), Washington University in Saint Louis, from May 1 to October 31, 2012. Patients had to be age 18 or older and admitted directly to the BJH neurology service from home, emergency department, or another hospital. Patients were excluded if they were cared for on another BJH service or in the neurocritical care unit prior to transfer to the neurology service, were admitted under 23-hour observation status or to the private neurology service, or were non-English speaking. Patients with aphasia or cognitive impairment could participate if a family member familiar with their hospital care was present.

Cases were screened by daily review of the discharge board and new admission list, supplemented by discussion with senior neurology residents, charge nurse, and social worker, as needed. Eligible patients or the patient’s caregiver were approached by a study team member not involved in the patient’s care within 24 hours of anticipated discharge and invited to participate in the study. The Washington University School of Medicine institutional review board approved this study, and verbal informed consent was provided by all participants or their caregiver.

All participants completed a questionnaire consisting of items addressing their knowledge of who their physicians were; which physician (if any) they believed knew them the best after the hospital stay; which physician (if any) they believed to be in charge of their care; and their level of satisfaction with their physician team using a 5-point Likert scale regarding overall care, communication, involvement in decisions, and being seen by the physician when needed. Along with the questionnaire, participants were provided with a composite containing names and photographs of all neurology attendings, fellows, and residents working on the inpatient neurology service that month.

Clinical descriptive data including date of admission, date of discharge, neurology team (general or stroke), primary discharge diagnosis, discharge disposition, age, sex, and insurance status were collected from the patient’s medical record. Names of all physicians on the neurology service who wrote daily notes or were directly involved in the patient’s care were recorded. Involvement of medical students and consultation by other services was noted, as were names of other physician team members the patient might have seen on morning rounds.

Two-tailed unpaired t tests were used to compare continuous variables, and Fisher exact test and χ² tests were used for noncontinuous variables. Descriptive statistics were used to analyze the patient identification data. All analyses were performed using GraphPad Instat version 3.1a for Mac OS X GraphPad Software, San Diego, CA (graphpad.com).

Results

Patient enrollment

A total of 1,460 patients were admitted to the neurology service during the study period. Of the 722 eligible for participation, 652 patients were enrolled. Reasons for non-enrollment included discharge before being able to complete the survey (n = 58) and refusal (n = 12). A small fraction of the enrolled patients (38/652) had the survey completed by a family member familiar with their hospital care.

Physician identification

An average of 3.9 (range 3–8) physicians were involved in each patient’s care. Patients were able to correctly identify on average 2.4 (60.7%) physicians involved in their care, and 93.2% of patients were able to identify at least one physician involved in their care. Patients were most likely to identify the junior resident as knowing them best and to identify the attending physician as being “in charge” of their care (figure).

Patient satisfaction

Three-quarters of the patients (494/652) answered “very satisfied” to all 4 survey questions related to satisfaction with care received by their physicians.
Patients with private insurance were more likely to be very satisfied (82.8% vs 70.5%, \( p < 0.001 \)). There was no difference in age, sex, length of stay, admission pathway, discharge disposition, primary diagnosis, student involvement, or person filling out the survey between the 2 groups (table).

Patients who were very satisfied were able to correctly identify a larger percentage of physicians involved in their care (63.8% vs 50.7%, \( p < 0.001 \)), were more likely to identify a physician who knew them best (94.3% vs 43.6%, \( p < 0.001 \) and a physician who was in charge of their care (94.1% vs 57.6%, \( p < 0.001 \), and were more likely to have fewer physicians involved in their care (3.84 vs 4.06, \( p = 0.02 \)).

**Discussion**

In this study, we found a patient’s satisfaction on an academic neurology inpatient service to be associated with their ability to identify the physicians involved in their care. In addition, we found associations between patient satisfaction and payer status and number of physicians involved in the patient’s care.

The link between a patient’s ability to identify the physicians involved in his or her care and degree of satisfaction is not surprising. Prior studies using open-ended questioning have found patients are rarely (~10%) able to identify at least one physician involved in their care.\(^3\)\(^,\)\(^4\) Using physician photograph composites, we achieved much greater identification in our study, with 93.2% of patients able to identify at least one physician, and on average, 60% of the physicians involved in their care. Indeed, providing patients with a photograph composite of providers may be a simple tool to improve patient satisfaction.\(^5\)\(^,\)\(^6\)\(^,\)\(^7\) In addition, writing the names of the patient’s providers in the room and structured/bedside handoffs are other simple interventions that may increase physician identification and ultimately improve patient satisfaction.

Satisfied patients were more likely to identify a physician who knew them best and a physician who was perceived to be “in charge” of their care, irrespective of the physician’s level of training. Not unexpectedly, the junior resident, who typically has the most face-to-face interaction with the patient, was most likely to be correctly identified. Furthermore, the junior resident was the physician most likely to be perceived as knowing the patient best. Since most patients believe it is important to know the level of training of a physician involved in their care\(^1\) but a majority do not understand the training hierarchy or physician roles in a teaching hospital,\(^3\)\(^,\)\(^4\) further research is needed to determine the influence that improving this understanding would have on satisfaction with care.

We also found patient satisfaction was associated with private insurance status, which has been reported by others.\(^8\) We cannot exclude the possibility of actual or perceived differential treatment based on insurance status as a contributor to this finding. Educating physicians about the implicit biases they may have and the influence of patients’ perception of bias on their health care could help reduce any disparities in care provided and potentially translate into improved patient satisfaction.

Finally, we found a relationship between number of physicians involved in a patient’s care and patient satisfaction. Although the absolute difference in number of physicians between patients who were very satisfied and those who were less than very satisfied is small (0.2), this finding highlights the influence that size of an academic team can have on overall patient satisfaction. While decreasing the number of physicians involved in a patient’s care in the academic setting may not be feasible given work-hour restrictions and need for trainee supervision, minimizing unnecessary handoffs could mitigate a potential cause of patient dissatisfaction, as could performance of structured handoffs at the bedside.\(^9\)
<table>
<thead>
<tr>
<th>Table: Predictors of patient satisfaction</th>
<th>Very satisfied</th>
<th>Less than very satisfied</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean (SD)</td>
<td>56.3 (16.6)</td>
<td>54.1 (18.4)</td>
<td>0.16</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td>0.14</td>
</tr>
<tr>
<td>Male (n = 315)</td>
<td>247 (78.4)</td>
<td>68 (21.5)</td>
<td></td>
</tr>
<tr>
<td>Female (n = 337)</td>
<td>247 (73.3)</td>
<td>90 (26.7)</td>
<td></td>
</tr>
<tr>
<td>Length of stay, d, mean (SD)</td>
<td>3.2 (2.0)</td>
<td>3.3 (1.7)</td>
<td>0.50</td>
</tr>
<tr>
<td>Insurance status, n (%)</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Private (n = 279)</td>
<td>231 (82.8)</td>
<td>48 (17.2)</td>
<td></td>
</tr>
<tr>
<td>Medicare/Medicaid/out-of-pocket (n = 373)</td>
<td>263 (70.5)</td>
<td>110 (29.5)</td>
<td></td>
</tr>
<tr>
<td>Admission pathway, n (%)</td>
<td></td>
<td></td>
<td>0.11</td>
</tr>
<tr>
<td>Emergency department (n = 400)</td>
<td>306 (76.5)</td>
<td>94 (23.5)</td>
<td></td>
</tr>
<tr>
<td>Transfer (outside hospital) (n = 180)</td>
<td>128 (71.1)</td>
<td>52 (28.9)</td>
<td></td>
</tr>
<tr>
<td>Direct admission (n = 72)</td>
<td>60 (83.3)</td>
<td>12 (16.6)</td>
<td></td>
</tr>
<tr>
<td>Discharge disposition, n (%)</td>
<td></td>
<td></td>
<td>0.79</td>
</tr>
<tr>
<td>Home (n = 468)</td>
<td>351 (75)</td>
<td>117 (25)</td>
<td></td>
</tr>
<tr>
<td>Inpatient rehabilitation (n = 148)</td>
<td>115 (77.7)</td>
<td>33 (22.3)</td>
<td></td>
</tr>
<tr>
<td>Skilled nursing facility (n = 34)</td>
<td>26 (76.5)</td>
<td>8 (23.5)</td>
<td></td>
</tr>
<tr>
<td>Primary diagnosis, n (%)</td>
<td></td>
<td></td>
<td>0.76</td>
</tr>
<tr>
<td>Vascular (n = 262)</td>
<td>204 (77.9)</td>
<td>58 (22.1)</td>
<td></td>
</tr>
<tr>
<td>Seizure (n = 82)</td>
<td>60 (73.2)</td>
<td>22 (26.8)</td>
<td></td>
</tr>
<tr>
<td>Headache/migraine (n = 47)</td>
<td>36 (76.6)</td>
<td>11 (23.4)</td>
<td></td>
</tr>
<tr>
<td>Multiple sclerosis/autoimmune (n = 37)</td>
<td>28 (75.7)</td>
<td>9 (24.3)</td>
<td></td>
</tr>
<tr>
<td>CNS infection (n = 26)</td>
<td>18 (69.2)</td>
<td>8 (30.8)</td>
<td></td>
</tr>
<tr>
<td>Nonepileptic seizure (n = 26)</td>
<td>18 (69.2)</td>
<td>8 (30.8)</td>
<td></td>
</tr>
<tr>
<td>Other (n = 162)</td>
<td>130 (80.2)</td>
<td>32 (19.8)</td>
<td></td>
</tr>
<tr>
<td>No. of physicians involved in care, mean (SD)</td>
<td>3.8 (1.0)</td>
<td>4.0 (1.2)</td>
<td>0.02</td>
</tr>
<tr>
<td>Consultant involved in care, n (%)</td>
<td>120 (24.3)</td>
<td>35 (22.2)</td>
<td>0.67</td>
</tr>
<tr>
<td>Student involved in care, n (%)</td>
<td>46 (9.3)</td>
<td>14 (8.9)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Family member completing survey, n (%)</td>
<td>25 (5.0)</td>
<td>13 (8.2)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

Our study was limited to identification of physicians, so we cannot address the influence on satisfaction of ability to identify other members of the patient care team. However, others have demonstrated enhanced satisfaction with nursing communication via use of posted names and photographs of nurses, suggesting our findings are not specific to physician identification.9

On an academic neurology inpatient service, patients who were more satisfied with their care were better able to identify the physicians involved in their care. Minimizing handoffs and coverage changes along with simple interventions to improve patient recognition of their physicians are potential strategies to enhance patient satisfaction. Such strategies are becoming increasingly important as academic centers contend with restriction in duty hours and as reimbursement becomes linked to patient satisfaction.

**Author contributions**

Christopher R. Leon Guerrero is responsible for manuscript drafting, acquisition of the clinical data, and evaluating and interpreting the data. Tracy Anderson is responsible for acquisition of the clinical data and revising the manuscript for intellectual content. Alyson R. Zazulia is responsible for study concept and design, acquisition of the clinical data, analysis and interpretation of the data, and revising the manuscript for intellectual content.
Study funding
No targeted funding reported.

Disclosure
The authors report no disclosures relevant to the manuscript.
Go to Neurology.org/N for full disclosures.

References

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Emerging Subspecialties in Neurology

These manuscripts will review the history and development of emerging subspecialties in neurology, including fields such as pain medicine, headache, neurocritical care, interventional neurology, and others. The focus should be on educating residents with a possible interest in this subspecialty. Those interested in writing these manuscripts should contact the Resident & Fellow Section editor before submission to inquire about the need for an article on a particular topic.
Emerging Subspecialties in Neurology: Pain medicine

Nathaniel M. Schuster, MD, and Jacob R. Hascalovici, MD, PhD

Correspondence
Dr. Schuster
rmschuster@ucsd.edu

Pain medicine is a multidisciplinary field specializing in the diagnosis and treatment of chronic pain anywhere in the body. Neurologists have a long history of contributions to the field of pain medicine, and in our experience, today’s generation of aspiring pain neurologists are finding ample opportunities for pain medicine fellowship positions as well as academic and non-academic pain medicine career opportunities upon graduation. Pain medicine is a rapidly evolving subspecialty that challenges practitioners’ cognitive, procedural, psychomotor, and interpersonal skills and offers a desirable work–life balance. Herein the authors provide a general overview of pain medicine as a neurologic subspecialty.

A brief history

In the United States, there are approximately 400 neurologists double board-certified in neurology and pain medicine. There is a notable history of neurologists as leaders in academic pain medicine and in industry. Silas Weir Mitchell, considered a father of American neurology, first described causalgia, now called complex regional pain syndrome type 2, in Union veterans following the US Civil War.1,2 Neurologists have been chiefs and former chiefs of academic pain medicine divisions, including David Borsook at Harvard’s Massachusetts General Hospital, R. Norman Harden at Northwestern’s Rehabilitation Institute of Chicago, Shaheen Lakhan at Virginia Tech Carilion, Charles Argoft at Albany Medical College, and Charles Brock at University of South Florida; the last 2 are based in neurology departments. In addition to the above individuals, other neurologists with notable contributions to the pain medicine literature have included Miroslav Backonja, Zahid Bajwa, Nathaniel Katz, Alyssa LeBel, John Markman, Anne Louise Oaklander, Michael Rowbotham, and many others not listed. Pain fellowship-trained neurologists are in high demand and currently employed at many academic medical centers including Massachusetts General Hospital, Boston Children’s Hospital, Brigham and Women’s Hospital, Boston University, Albert Einstein College of Medicine, Albany Medical College, University of Rochester, Virginia Tech Carilion, University of South Florida, Mayo Clinic in Rochester, University of Washington, Stanford University, University of California, San Francisco, University of California, Los Angeles, and University of California, San Diego. A list of pain fellowship-trained neurologists that we are aware of (likely an incomplete list) on faculty at academic medical centers as of July 2018 can be found in table 1.

Practice parameters and the scope of pain neurology

Pain neurologists treat highly prevalent and disabling disorders. Lower back and neck pain has been the leading cause of disability in every Global Burden of Disease Study (GBD) from 1990 to 2015. In 2015, the GBD ranked other musculoskeletal disorders the 8th leading cause of disability, while migraine ranked 7th, and medication overuse headache 20th.3

Pain medicine practice is primarily outpatient-based with regular weekday hours and a mix of clinic and procedural time. An average week as a pain medicine physician will include clinic visits with patients with axial and radicular neck and lower back pain, musculoskeletal pain, neuropathic pain, and headache, and performing diagnostic and therapeutic fluoroscopic and ultrasound-guided procedures including epidural steroid injections, joint and bursa injections,
diagnostic facet or medial branch blocks and radiofrequency ablations, sympathetic blocks, as well as non-image-guided procedures including chemodenervation for chronic migraine, occipital and trigeminal nerve blocks, and trigger point injections. Many pain physicians are also trained in advanced percutaneous interventional therapeutics for chronic pain including neuromodulation (such as spinal cord stimulation, dorsal root ganglion stimulation, and peripheral nerve stimulation), intrathecal pump placement and management, and vertebral augmentation procedures. Depending on the position, there may be inpatient consultations as part of the job responsibilities, but these are usually nonemergency consultations. Emergencies in pain medicine are rare but may include cancer pain crises, pediatric pain crises, and intrathecal pump malfunction.

While pain medicine is most often associated with performing interventional spine, muscle, nerve and joint procedures, pain medicine practice also includes oral and topical pharmacotherapy and referrals to colleagues for treatments including physical therapy, multimodal functional restoration programs, acupuncture, pain psychology, pain psychiatry, biofeedback, mindfulness meditation training, and osteopathic manipulation. Also, with the ongoing opioid epidemic, pain medicine physicians are called upon to help primary care doctors wean patient’s opioids through the use of multimodal care.

Residency prepares neurologists for outpatient clinic life with regards to obtaining an expert history and physical examination, critically evaluating results from diagnostic testing, and providing a thoughtful assessment and plan. Pain neurologists also serve a valuable function in academia teaching about neurologic disorders (especially headache, peripheral neuropathies, and sympathetically mediated pain syndromes), neurologic examination, and reading and interpreting neuroaxial imaging studies. In the case of possible postprocedural complications (including nonphysiologic adverse events), colleagues may call on the pain neurologist to provide an expert neurologic examination and assessment. In most pain medicine groups, a trained neurologist is a rare commodity and pain fellows who are trained in neurology bring valuable knowledge and skills to their pain medicine faculty and cofellows.

Furthermore, since headache is so highly prevalent in the overall population but headache specialists are in short supply, pain neurologists often serve as de facto headache and facial pain specialists in their institutions.

### Pain medicine fellowship

There are 102 Accreditation Council for Graduate Medical Education (ACGME)-accredited pain medicine fellowships in the United States, as well as numerous unaccredited fellowships. Of these 102 fellowship programs, 98 programs participated in the national resident match program in 2017 to fill 335 positions. Match rates from 2017 are listed: 231 of 287 (80.5%) US medical school graduates and 335 of 438 (76.5%) total applicants successfully matched. Most applicants match

<table>
<thead>
<tr>
<th>Institution</th>
<th>Faculty members</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harvard University (Boston Children’s Hospital, Brigham and Women’s Hospital, Massachusetts General Hospital)</td>
<td>David Borsook, MD, PhD; Pradeep Dinakar, MBBS; Alyssa LeBel, MD; Anne Louise Oaklander, MD, PhD; Brian Walinger, MD, PhD; Victor Wang, MD, PhD</td>
</tr>
<tr>
<td>Louisiana State University</td>
<td>Harry J. Gould, MD, PhD</td>
</tr>
<tr>
<td>Boston University</td>
<td>Michael Perloff, MD, PhD</td>
</tr>
<tr>
<td>Albert Einstein College of Medicine</td>
<td>Jacob Hascalovici, MD, PhD</td>
</tr>
<tr>
<td>Albany Medical College</td>
<td>Charles Argoff, MD</td>
</tr>
<tr>
<td>University of Rochester</td>
<td>John Markman, MD</td>
</tr>
<tr>
<td>University of South Florida</td>
<td>Charles Brock, MD</td>
</tr>
<tr>
<td>Mayo Clinic Rochester</td>
<td>Narayan Kissoon, MD; James Watson, MD</td>
</tr>
<tr>
<td>University of Washington</td>
<td>Miroslav Backonja, MD</td>
</tr>
<tr>
<td>Stanford University</td>
<td>Meredith Barad, MD</td>
</tr>
<tr>
<td>University of California, San Francisco</td>
<td>Cindy Chai, MD; Prasad Shirvalkar, MD, PhD</td>
</tr>
<tr>
<td>University of California, Los Angeles</td>
<td>Chelsea Hesterman, MD; Mollie Johnston, MD</td>
</tr>
<tr>
<td>University of California, San Diego</td>
<td>Imanuel Lerman, MD; MS; Nathaniel Schuster, MD</td>
</tr>
<tr>
<td>Virginia Tech</td>
<td>Shaheen Lakhan, MD</td>
</tr>
</tbody>
</table>
to one of their top choices, as 45.2% matched to their top choice, 11.2% to their second choice, 7.3% to their third choice, and 11.2% to greater than third choice. Twenty-four percent of applicants did not match. The authors are unaware of publicly available data regarding pain medicine fellowship match rates stratified by background residency training (i.e., neurology, anesthesiology, psychiatry, psychology).

Neurologists are matching to pain fellowships with the highest academic profiles disproportionate to neurologists’ prevalence in the overall applicant pool. For example, during the 2016–2017 academic year, neurologists represented 1 out of the 7 pain fellows at Massachusetts General Hospital, 1 out of the 9 pain fellows at Brigham and Women’s Hospital, and 1 out of the 5 pain fellows at UCSF, while neurologists were likely about 1%–2% of the total pain fellow applicant pool that year. While the data are not available, neurologists may out-perform the overall pain fellowship applicant pool because applications from neurologists stand out due to their scarcity. The programs with the highest academic profiles appear to seek neurologists to build well-rounded fellowship classes.

A sample application timeline for neurology resident application preparation is provided in table 2.

Although neurologists, via the American Board of Psychiatry and Neurology (ABPN), belong to one of the 6 boards that cosponsor the pain medicine board certification (the others being anesthesiology, psychiatry, psychiatry, emergency medicine, and family medicine), the vast majority of pain medicine fellowship applicants in the United States are anesthesiologists and psychiatrists. According to data obtained from 3 program directors of large ACGME-accredited pain fellowship programs, during the 2018 application cycle, the 3 programs combined received a total of 780 applications, of which only 10, or 1.2%, were from neurologists; the authors acknowledge the limitation of likely duplicates in the applicant pools (personal communication, Gary Brenner, MD, PhD; Timothy Furnish, MD; and Sayed Emal Wahezi, MD). Pain fellowships are mostly based within anesthesiology or physical medicine and rehabilitation departments, but the pain medicine departments at both the Albany Medical College and the University of South Florida are based in neurology departments. More important than the home department is the philosophy of the department. A growing number of anesthesiology- or psychiatry-based pain fellowships have trained neurologists in the past and have one or more pain-trained neurologists on faculty. With the ongoing opioid epidemic in the United States, today many pain medicine fellowship programs emphasize non-opioid-based pharmacologic treatments for chronic pain, as well as education in opioid tapering and cessation. Inpatient consultations for acute pain are a core requirement of all ACGME-accredited pain medicine fellowships, although this is usually much lighter than the inpatient consultation requirements of a general neurology resident.

Regardless of whether the fellowship is based in an anesthesiology, psychiatry, or neurology department, the pain medicine boards are administered annually in September, and neurologists sign up for the pain medicine boards via the ABPN.

Research opportunities

Like neurology and neurosciences in general, the field of pain medicine is continuously evolving. The opioid epidemic is adding to the urgency of better understanding chronic pain and advancing new nonopioid pain treatments. For neurologists interested in research, there are opportunities in basic science and clinical and translational research. Functional neuroimaging, headache and facial pain, central pain syndromes, and neuromodulation are several lines of clinical research that may be especially well-suited to neurologists given their knowledge of neuroanatomy and neurophysiology, comfort level in diagnosing and treating neurologic disorders, and experience reviewing and interpreting neuroimaging studies.

Pain medicine is an exciting hands-on subspecialty available to neurology residents. While neurology residents may feel that opportunities in pain medicine for neurologists are scarce, the authors have found the opposite is true: neurologists interested in pain medicine are a rare commodity that is in high demand for both fellowship positions and pain faculty

Table 2: Timeline for applying for ACGME-accredited pain fellowships

<table>
<thead>
<tr>
<th>Timing</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>July of PGY-3 year (or 2 years before one hopes to begin fellowship)</td>
<td>Ask faculty for at least 4 letters of recommendation. Consider obtaining from at least one pain physician and one headache specialist.</td>
</tr>
<tr>
<td>December 1 of PGY-3 year</td>
<td>Applications open via ERAS</td>
</tr>
<tr>
<td>May of PGY-3 through August of PGY-4 year</td>
<td>Interviews</td>
</tr>
<tr>
<td>Late September or early October of PGY-4 year</td>
<td>Rank list deadline via NRMP</td>
</tr>
<tr>
<td>Mid-October of PGY-4 year</td>
<td>Match day</td>
</tr>
</tbody>
</table>

Abbreviations: ACGME = Accreditation Council for Graduate Medical Education; ERAS = Electronic Residency Application Service; NRMP = National Resident Matching Program; PGY = postgraduate year.
positions. Understanding factors involved in neurology residents’ awareness of and barriers to pursuing pain medicine fellowships is deserving of future research.

References

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Global and Community Health

More than 85% of the world’s population lives in low and middle income countries, where the burden of neurologic disease is greatest. In addition, over 50 million Americans live in medically underserved communities. Despite these figures, relatively little is known about patients and practitioners of neurology in resource-limited settings. This section aims to explore global and community health topics in neurology education. We welcome manuscripts describing international educational exchanges, personal rotations in low and middle income countries, and work by neurology trainees from around the world. We also welcome manuscripts that discuss community health initiatives and volunteer experiences in underserved regions of the United States. Inclusion of practical information on local or international volunteer opportunities would also be of use.
International Issues: A guide to US academic global health programs in neurology

Rohini D. Samudraiwarr, MD, Adeline Goss, MD, Kathryn Rimmer, MD, Kara Shetler, MD, Allison Navis, MD, Omar K. Siddiqi, MD, MPH, Jerome H. Chin, MD, PhD, MPH, and Kiran T. Thakur, MD


Global health programs advocate for a better understanding of health disparities, often prompting medical trainees to practice medicine in an international setting. The relevance of global health electives in neurology is highlighted by the increasing burden of neurologic diseases in low- and middle-income countries (LMICs), representing 84% of the world’s population.1,2 Cerebrovascular disease is the second leading cause of morbidity and mortality worldwide, and dementia, meningitis, migraine, and epilepsy are in the top 50 factors in disability-adjusted life years. Neurologists therefore play a key role in global health, caring for patients with acute neurologic disorders and neurologic sequelae of both noncommunicable and communicable diseases. Despite this, there are only 0.03 to 1.09 neurologists per 100,000 people in LMICs, with large inequalities in access to care, compared to 4.75 per 100,000 population in high-income countries.3 Through developing collaborative relationships and a cross-cultural exchange of knowledge, US neurology trainees can play a role in addressing these disparities in neurologic care.

Many US neurology residency programs have developed global health programs that can provide a mutually beneficial exchange of resources and training programs between partner institutions in one or more LMICs. Federal and foundation funding has increased over the last decade, extending support to subspecialties in neurology including movement disorders, neuroinfectious disease, epilepsy, and stroke.4 For trainees, these placements can expand knowledge of neurologic diseases, improve clinical skills, and help develop an appreciation of public health, cultural, and socioeconomic issues affecting the population of the partner country.5 The host institution is supported through clinical teaching of local health care personel, patient care, and research.

The Global Health Section of the American Academy of Neurology (AAN) has established a network of neurologists within the AAN to advance international collaborations and to foster global health interest among neurology trainees in the United States and other countries. The Section includes 443 members, and is one of the fastest growing sections of the AAN particularly among trainees. One critical goal is to connect US neurology trainees with clinical and research opportunities in LMICs, and to develop mutually beneficial exchanges that can ultimately improve neurologic care in resource-limited settings. To facilitate this, the Global Health Section of the AAN has compiled a list of available global neurology electives for interested trainees (appendix e-1, links.lww.com/WNL/A326). Information gathered for appendix e-1 was through a request via email and discussion through Synapse AAN Online Communities to members of the AAN global health section. While this is not a complete list, it provides a sample of programs, which have been made available through the AAN. This article offers predeparture, funding, and postdeparture advice to ensure a meaningful elective rotation focused on mutual enrichment of home and host institutions.
Selecting a program

Programs in global neurology vary in focus, duration, and trainee level. In selecting a program, trainees often choose between a clinical or research focus. This decision will help narrow the search for programs and guide further logistical planning. It is important to note that many clinically oriented programs may still encourage a small-scale project, such as a prospective case series or evaluation of practice patterns or resources. Some may also incorporate training of local health care providers including nurses and physician extenders.

Region and language barriers can also play a role in decision-making. The importance of language skills depends on the duration of the trip and the type of project the trainee intends to pursue. For any in-depth research or clinical experience, trainees should strongly consider working in a location where they have familiarity with the local language. This is important both to maximize their productivity and to minimize burden on the host institution.

Once a trainee identifies the preferred focus and geographic region, he or she can begin to search for specific programs. We offer the attached appendix e-1 (links.lww.com/WNL/A326) as a starting point for medical students, residents, and fellows, as well as the figure as an example timeline in preparation for a global health rotation. Many programs are geared towards senior neurology residents, while others are available to trainees across all levels. This list is not comprehensive, and we encourage trainees to explore advertised and unadvertised opportunities at their home institutions, as well as those with the NIH and nongovernmental organizations.

Predeparture planning

Early planning is the key to a successful global health rotation. This is particularly true for residents and fellows. Residents may find it difficult to schedule an international elective, in part because the Accreditation Council for Graduate Medical Education requires participation in a continuity clinic throughout training. Fellows have a similar challenge scheduling around duties. It is important to discuss the timing of a global health project with one’s program director, administrative director, and chief resident to schedule clinic-free and call-free electives. More than a year of planning may be necessary. Programmatic approval as well as compliance with ACGME takes a significant amount of time, and trainees should be in close communication with their administrative director of education to facilitate necessary paperwork for approvals 1 year prior to departure. Trainees meeting challenges may benefit from structuring their global health work as part of their protected research time or as a grant-funded project; this may ensure dedicated time to a global health program without missing local resident or fellow duties.

Identifying mentors at home and host sites is another key step in planning a meaningful international elective. At home institutions, US trainees should seek out at least one mentor with substantial global health experience who can provide advice on rotation structure, logistics, and cross-cultural issues. Ideally, this mentor will have an established relationship with the partner institution. Trainees should also identify a neurologist at their home institution (not necessarily the same individual) who shares their clinical or research interests and can help develop the specifics of the elective. In the programs listed in appendix e-1 (links.lww.com/WNL/A326), many have trained neurologists or other physicians designated to oversee activities in the host countries. In addition, a host site coordinator who can assist with the required documentation for medical licensing (if required), malpractice, housing, local transportation, and safety should be identified. A faculty mentor at the visiting institution is often required for supervision and evaluation of the trainee.

In preparation for the visit, trainees should refresh their training in cultural humility, cross-cultural communication (including working with interpreters), medical ethics, and unconscious bias. Many programs have required global health courses and predeparture training on one or more of these topics. Mentors can assist with orienting the trainee to specific cultural norms and geopolitical issues in the country he or she will be visiting.

Travel safety and health

For resources on travel security, the US Department of State’s website has updated country-specific travel warnings and alerts. Updated information on country-specific travel health alerts, vaccinations, and prophylaxis is available at the Centers for Disease Control and Prevention website. Some vaccinations may need to be administered 4–6 weeks in advance of arrival to the host country and an appointment with a travel medicine expert is recommended at least 6 months prior to travel. Trainees should plan to bring their own antiretroviral medications for postexposure prophylaxis if not readily available in host country. A 4-week supply can be prescribed by a trainee’s physician. Evacuation insurance can also be purchased in case of medical emergencies. This may be provided as a supplement to existing insurance for an additional fee or free of charge with affiliated institution.

Travel documents

It is important to have a valid passport that is not due to expire within 6 months of foreign site arrival or departure. In addition, some countries in South America, Africa, the Middle East, South East Asia, and Oceania require a visa upon entry for holders of a US passport. Country-specific visa application requirements are available at the US Department of State’s website. It is recommended that at least 3–4 months be allocated for securing a passport or visa.

Institutional review board

For research projects, the process of institutional review board (IRB) approval may involve review by both US and partner institutions. Of note, some project proposals may be exempt from IRB approval, but should be confirmed through formal IRB processes. In addition, IRBs in the United States
generally conduct reviews based on different ethical schemas (e.g., the Common Rule) than those in other countries (e.g., the Declaration of Helsinki). For these reasons, the researcher should contact both institutions well before departure to clarify application requirements for approval or exemption. Research mentors can provide guidance in these cases.

**Funding**

Estimating project expenses is a fundamental aspect of pre-departure planning. Costs may include materials (e.g., laboratory equipment, clinical instruments, fuel and food for volunteer collaborators traveling to project sites) and services (e.g., translation fees, printing, data analysis) required to carry out the project. Other costs include personal expenses, such as housing, food, transportation, passport or visa fees, predeparture vaccinations, and prophylactic medications. Requirements for a national medical license and malpractice insurance vary by location and may pose additional costs.

Many programs listed in appendix e-1 (links.lww.com/WNL/A326) offer limited funding. Trainees should reach out to their residency program directors or medical school global health office to inquire about internal grants or scholarships for independently organized projects. If these are nonexistent or inadequate, external programs should be considered (table e-1, links.lww.com/WNL/A325). Stipulations on the allocation of funds vary by source, and the trainee should be prepared to pay for a portion of ancillary expenses with personal funds. For research projects, it may be possible to apply for grants or obtain sponsorship through a mentor. Once the project is underway, the trainee should document all expenses carefully and keep itemized receipts, as some funding sources may require these for reimbursement. Once budget estimates and funding sources are determined, the trainee will need a US bank account with reliable access to funds in the destination country. Automated teller machines or money transfer accounts such as Western Union can be useful methods to access funds internationally. Another option is to open an account at an international bank with branches in the rotation site.

**Telecommunications**

It is crucial to establish telecommunication as early as possible. If the trainee has a smartphone, it can be unlocked during the
predeparture period and used to operate an international SIM card giving the trainee access to the cellular network (i.e., phone, SMS, and data) of the destination country. Alternatively, an inexpensive mobile phone and SIM card can often be purchased locally. Internet access can also be an issue and although some areas may provide wifi, this is not always dependable.

**Arrival and troubleshooting**

Establishing contact with the host coordinator upon arrival can address any issues with housing, transportation, or telecommunications. In addition, access to site facilities and familiarity with surroundings can ease the transition to an international environment. Throughout the course of the elective, it is imperative to designate time and maintain contact with mentors to meet the goals of a research project or clinical activity. This will also address issues early, allowing for a more successful outcome. Creating a log of patients, procedures, and experiences will provide a reference for personal education and can facilitate postdeparture debriefings with home institutions.

**Postdeparture debriefing**

After the trainee’s elective is completed, it is important to debrief with mentors at both home and partner institutions to review the strengths, weaknesses, and future directions of the collaboration. This facilitates growth on both institutional and personal levels by translating partnerships into insight and self-improvement. Some programs may require presentations and research to be shared with the neurology department and other audiences. Regardless of a project’s measurable outcomes (e.g., adequate research data collection, successful establishment of clinical programs), its legacy derives from the strengthening of institutional relationships and successful reporting back of individual experiences. Connections with the host institution should be continued through email and teleconferences to continue sharing knowledge and experiences. Ideally a trainee will be able to practice at the site not only once, but establish a longitudinal relationship. Additionally, exchange opportunities should be implemented if available.

**Discussion**

Global health activities offer US neurology trainees opportunities to expand their clinical and research knowledge and skills, develop an informed appreciation of global health disparities, and interact with clinicians and researchers in LMICs. The discipline of global health is evolving, and the opportunities for training abroad are likely to grow as there is increased recognition of global health disparities in neurology.

**Author contributions**

Dr. Samudralwar: acquisition of data, original manuscript draft, critical revision of the manuscript. Dr. Goss: original manuscript draft, critical revision of the manuscript. Dr. Rimmer: acquisition of data, original manuscript draft, finalization and verification of appendix, revision of the manuscript. Dr. Shetler: acquisition of data, original manuscript draft, finalization and verification of table, revision of the manuscript. Dr. Navis: original manuscript draft, revision of the manuscript. Dr. Siddiqi: critical revision of the manuscript. Dr. Chin: critical revision of the manuscript. Dr. Thakur: study supervision, critical revision of the manuscript.

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Amy C. Lee, MD, MPH (Palo Alto Medical Foundation, Mountain View, CA) and Ana-Claire L. Meyer, MD (Senior Clinical Advisor at US Army, Medical Research and Material Command and Adjunct Assistant Professor, Yale School of Medicine, New Haven, CT) developed the original list and information of global health programs in appendix e-1 (links: lww.com/WNL/A326). Members of the Global Health Section of the AAN who provided institutional and affiliate information to assemble appendix e-1.

**Study funding**

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**Disclosure**

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**References**

Neurology Journal Club

Neurology® Journal Club submissions are structured evaluations of recent Neurology research articles. The aim is to enhance the training of residents and fellows by instruction in the critical appraisal of medical literature. Residents or fellows interested in submitting a Neurology Journal Club article should review the e-Publication Ahead of Print articles at NPub.org/aheadofprint for the most recently published material and email Neurology with their selection for prior approval. Selections will aim to represent the major categories of research methodology over the course of a three-year residency cycle. Submissions should be timely and are requested no longer than four weeks following the original e-publication date of the subject article. These Journal Club critiques, written by neurology residents and fellows with faculty supervision, should follow a specific outline and contain subtitles for background and significance, hypothesis and design, methods, results, and interpretation. Rather than a critical correspondence or editorial, this feature will highlight methods for the critical appraisal of medical literature. This online feature could be used as an adjunct to traditional institutional journal clubs and promote discussion among neurologists, including trainees and those in practice.
Journal Club: Florbetapir imaging in cerebral amyloid angiopathy-related hemorrhages

Andreas Charidimou, MD, PhD, Anne-Katrin Giese, MD, Marco Pasi, MD, Susanne J. van Veluw, PhD, Li Xiong, MD, PhD, Panagiotis Poliadis, BSc, Sandro Marini, MD, Markus D. Schirmer, PhD, and Anand Viswanathan, MD, PhD

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Cerebral amyloid angiopathy (CAA) is a common type of cerebral small vessel disease and a key cause of spontaneous lobar intracerebral hemorrhage (ICH) in the elderly.1,2 Currently, the clinical diagnosis of probable CAA is based on characteristic imaging findings including strictly lobar ICH and CAA-associated hemorrhagic lesions (e.g., cerebral microbleeds [CMB] and cortical superficial siderosis). Despite their high specificity for CAA,3 these lesions only provide indirect evidence of advanced disease. Currently, a definite CAA diagnosis can only be obtained on a brain biopsy or with a neuropathologic examination of the brain postmortem. Quantifying potential early stages of CAA in vivo through more direct biomarkers remains challenging.4 In order to assess the diagnostic yield of a direct amyloid PET tracer in the clinical setting, in the Journal club article “Florbetapir imaging in cerebral amyloid angiopathy-related hemorrhages,” Raposo and colleagues compared cortical florbetapir-PET retention between patients with CAA-related ICH and patients with hypertension-related deep ICH. The authors report increased cortical florbetapir-PET uptake in patients with CAA-related ICH compared to those with deep ICH. However, its diagnostic value in acute CAA-related ICH was proved to be limited by its moderate sensitivity and specificity. While these data do not yet have direct implications for CAA in clinical practice, they are useful in consolidating evidence on amyloid-PET performance in the setting of symptomatic CAA-related lobar ICH and may be informative for guiding future studies and trials in CAA.4

Hypothesis and design

The authors hypothesized that patients with CAA-related ICH may have higher cortical florbetapir retention and an occipital predominance compared to patients with deep ICH. They hypothesized that the increased retention may provide high diagnostic value to identify those ICH patients with CAA. The study prospectively enrolled 33 patients with acute symptomatic ICH from a single center.

Methods

This case-control study prospectively enrolled patients with acute spontaneous symptomatic ICH and classified them into 2 groups: lobar ICH patients fulfilling the modified clinical-MRI Boston criteria for probable CAA5,6; and deep ICH, as a comparison group. Patients with preexisting cognitive impairment, as determined by a score of ≥3.4 on the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), were excluded from the study. All patients had to have undergone 3T MRI with blood-sensitive sequences (i.e., T2*‐weighted gradient-recalled echo), to allow for CAA classification according to the Boston diagnostic criteria, and based on the presence of strictly lobar CMB, a putative hemorrhagic small vessel disease marker. Patients underwent 3T MRI approximately 15 days post-ICH (median, interquartile range [IQR] 9–28 days). MRI scans were then used to classify patients and assess small vessel disease neuroimaging markers according to Standards for Reporting

From the Hemorrhagic Stroke Research Program, Department of Neurology, Massachusetts General Hospital Stroke Research Center, Harvard Medical School, Boston.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.
Vascular Changes on Neuroimaging recommendations, blinded to all other clinical or PET data.

To examine the burden and regional pattern of amyloid in the brain of these patients, the authors appropriately performed amyloid-PET imaging with $^{18}$F-florbetapir at an average 39 days (IQR 21–93 days) post-ICH, using standard methodology. Data were processed using FSL (fmrrib.ox.ac.uk/fsl) in 3D T1-weighted images. Probability maps were generated using the FMRIB Automated Segmentation Tool (FSL library tools) using appropriate standard thresholding, coregistration of CT scan space onto T1 space, transformation matrices, and anatomic regions of interest (ROIs). Global cortical and regional standardized uptake value ratio (SUVr) of florbetapir, which allows quantification of amyloid burden in the brain, was analyzed for each patient and compared between the 2 groups using $t$ tests.

Florbetapir mean cortical retention was compared in 15 patients with acute CAA-related lobar ICH (mean age 63.7 ± 12, 40% female) and 18 patients with acute hypertension-related deep ICH (mean age 63.1 ± 11, 27.8% female). The contralateral (i.e., ICH-free) hemispheres of all participants were blindly assessed by 2 independent raters (who showed excellent interrater agreement, $\kappa = 1$), categorizing the PET florbetapir images as either florbetapir-positive or florbetapin-negative. To assess the performance of florbetapir, the area under the curve (AUC) and sensitivity and specificity for global florbetapir were estimated.

For basic definition of the terms mentioned in the article, see the table.

### Results

The main results were that cortical florbetapir-PET uptake was increased in patients with CAA-related ICH compared to those with deep ICH. The 2 ICH groups were similar in their vascular risk factor profile (compared using Student $t$ tests or Mann-Whitney $U$ tests for normally and non-normally distributed continuous variables and $\chi^2$ tests for categorical variables) with the exception of hypertension and APOE genotype. Hypertension was more prevalent in the deep ICH group and the APOE $\varepsilon2$ or APOE $\varepsilon4$ genotype was more prevalent in the CAA-ICH cohort. These differences in clinical characteristics are expected, given that the majority of deep ICHs are driven by hypertension or associated with vascular risk factor pathologies, while APOE is implicated in vascular amyloid accumulation pathophysiology.

Global cortical florbetapir retention was higher in CAA-ICH patients compared to deep ICH patients (SUVr 1.27 ± 0.12 vs 1.12 ± 0.12, $p = 0.001$, Cohen $d = 1.25$). Similarly, in univariable regional ROI analysis, florbetapir retention was higher in all individual cortical regions of the CAA-ICH patients when compared to the deep ICH patients. Among patients with CAA, the highest SUVr was estimated in the occipital lobe (1.31 ± 0.16). Of note, the occipital/whole cortex ratio was not different between CAA-ICH vs deep ICH patients (1.03 ± 0.07 vs 1.02 ± 0.05, $p = 0.656$).

The AUC for distinguishing CAA-ICH and deep ICH was 0.811 (95% confidence interval [CI] 0.642–0.980). At the SUVr threshold of 1.18, the sensitivity to differentiate CAA-ICH and deep ICH was 0.733 (95% CI 0.475–0.893) and the specificity was 0.833 (95% CI 0.598–0.948). Of all CAA-ICH patients, 60% (95% CI 0.352–0.848) were florbetapir-positive, in comparison to only 11% (95% CI 0.034–0.256) in the deep ICH group, based on visual analysis.

### Discussion

The authors explored florbetapir, a well-established amyloid radioligand commonly used in Alzheimer disease, and examined its presence and spatial distribution in acute CAA-ICH patients vs deep ICH patients. The study confirms recent findings that florbetapir binding is increased in patients with CAA-related lobar ICH compared to patients with hypertension-related deep ICH. The authors appropriately conclude that the use of florbetapir-PET does not seem to increase sensitivity or specificity for CAA diagnosis, beyond the modified Boston criteria, and therefore has limited diagnostic value in clinical practice. Key strengths of the study include the combination of MRI and PET in the first weeks after ICH to evaluate CAA and comprehensive data on sensitivity and specificity of florbetapir to evaluate this new tracer as a potential diagnostic tool for the in vivo identification of CAA.

The findings of this interesting and elegant study need to be considered in the context of potential limitations, some of which are inherent to amyloid-PET studies in the field, while others are more related to the selected methodology. The main points relevant for interpretation include the following:

1. The selection of the study sample may have resulted in a potential selection bias, which potentially limits generalizability of the results. For example, the reported mean NIH Stroke Scale score and hematoma volumes are relatively low, suggesting a clinically mild ICH population. The mean age of this sample is also relatively low (63.7 years), compared to previously reported CAA cohorts (~70 years). PET imaging is likely better tolerated in relatively young and mildly affected patients with ICH. These factors may limit the study’s generalizability, and hence these results might only be applicable to selected clinically mild ICH cases that do not represent the main bulk of patients seen in stroke clinics.

2. The selection of the deep ICH comparison group raises some concerns. Patients who presented with deep ICH who happened to have lobar CMBs may have been included in the control group since lobar CMBs are not
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tr>
<td><strong>Small vessel disease terms</strong></td>
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<tr>
<td><strong>Cerebral amyloid angiopathy</strong></td>
<td>A chronic degenerative disease characterized by progressive deposition of β-amyloid in the media and adventitia of leptomeningeal vessels, small arteries, arterioles, and sometimes capillaries in the cerebral cortex. It commonly results in strictly lobar intracerebral hemorrhage and cerebral microbleeds in the elderly.</td>
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<td><strong>Cerebral microbleeds</strong></td>
<td>Small (generally 2–5 mm in diameter, but sometimes up to 10 mm) areas of signal void with associated blooming seen on T2*-weighted MRI or other sequences that are sensitive to susceptibility effects. Results of some studies suggest that MRI-visible microbleeds correspond to hemosiderin-laden macrophages in perivascular tissue, consistent with vascular leakage of blood cells affected by small vessel disease.</td>
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<td><strong>Imaging analysis terms</strong></td>
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<tr>
<td><strong>Segmentation</strong></td>
<td>Dividing a scan (i.e., T1-weighted) into multiple anatomic structures of interest.</td>
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<tr>
<td><strong>Gray matter probability map</strong></td>
<td>Maps where the intensity value of each voxel (i.e., 3D pixel) represents the probability that it belongs to gray matter.</td>
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<tr>
<td><strong>Registration</strong></td>
<td>Aligning an MRI sequence to another sequence using a transformation matrix, as to establish direct correspondence between their anatomical features.</td>
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<tr>
<td><strong>PET</strong></td>
<td>A nuclear medicine functional imaging technique that is used to observe metabolic processes in the body. The system detects pairs of gamma rays emitted indirectly by a positron-emitting radionuclide (tracer), which is introduced into the body on a biologically active molecule. 3D images of tracer concentration within the body are then constructed by computer analysis.</td>
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<tr>
<td><strong>18F-florbetapir</strong></td>
<td>PET scanning radioligand compound containing the radionuclide fluorine-18; recently Food and Drug Administration–approved as a diagnostic tool for Alzheimer disease. Florbetapir, like Pittsburgh compound B (PiB), binds to β-amyloid; however, fluorine-18 has a half-life of 109.75 minutes, in contrast to PiB’s radioactive half-life of 20 minutes.</td>
</tr>
<tr>
<td><strong>Statistical terms</strong></td>
<td></td>
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<tr>
<td><strong>Specificity</strong></td>
<td>True negative rate: Number of true negatives/(number of true negatives + number of false-positives).</td>
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<tr>
<td><strong>t Test</strong></td>
<td>Statistical test most commonly applied when the test statistic would follow a normal distribution. The test can be used, for example, to determine if 2 normally distributed sets of data are significantly different from each other.</td>
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<tr>
<td><strong>Receiver operating characteristic (ROC)</strong></td>
<td>An ROC curve plots true positive rate (sensitivity) and false-positive rate (100 – specificity) against each other. The closer the curve is to the upper left corner, the higher is the accuracy of the measure tested.</td>
</tr>
<tr>
<td><strong>Area under the curve (AUC)</strong></td>
<td>An AUC measures performance of a measure (how well measure can distinguish case/control or disease/normal). AUC can range from 0.5 (no better than chance) to 1 (perfect classification).</td>
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been interesting in disentangling the burden and patterns of florbetapir-PET.8

Beyond these limitations (many of them thoroughly discussed in the article), this work is important for the advancement of the field and will be useful in informing future studies on the diagnostic yield of amyloid-PET in CAA. Overall, the results point to the general consensus of the use of amyloid-PET in the setting of symptomatic CAA: a negative florbetapir-PET scan in a case with lobar or deep hemorrhages may rule out CAA as the underlying etiology, but a positive florbetapir-PET scan remains challenging to interpret, since the signal may come from vascular or parenchymal amyloid deposits. The interested reader is directed to a recent systematic review of amyloid-PET studies in CAA, including gaps and directions for future research in the field.8

Author contributions

Study funding
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Disclosure
The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

References

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Mystery Case

Interesting teaching cases submitted to the Resident & Fellow Section are chosen by the editors to be published under the new Mystery Case subcategory. The Neurology® editorial office disseminates a teaser through social media before the case is published. This usually includes a short description of the case, video or partial figure, and one to three questions. Responses are compiled and then published with the full case.
Mystery Case: Tortuous hairs and tortuous blood vessels

Indar Kumar Sharawat, MD, Renu Suthar, DM, Sameer Vyas, MD, Amit Rawat, MD, and Naveen Sankhyan, DM

Neurology® 2018;90:e1174-e1176. doi:10.1212/WNL.0000000000005208

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Figure 1 Clinical features and hair microscopy

(A) Facial appearance: thin, sparse, short, silvery, wiry hairs and epicanthus.
(B) Loose skin folds over dorsum of hand. Hair microscopy: (C) pili torti (180-degree twisting of hair shaft) and (D) trichorrhexis nodosa (formation of nodes along the hair shaft with breakage).

A 5-month-old boy, born to a third-degree consanguineous couple, presented with drug-refractory seizures. On examination, he had microcephaly, abnormal scalp hairs (figure 1A), loose skin folds (figure 1B), and generalized hypotonia. Based on hair microscopy (figure 1, C and D), radiologic findings (figure 2, A–D), and a pathogenic mutation in the ATP7A gene (c.4006-1G>C, intron 20), a diagnosis of Menkes disease was confirmed.

Discussion
Dysfunction of multiple copper-dependent enzymes in Menkes disease, like lysyl oxidase (crosslinks elastin) and sulfhydryl oxidase (crosslinks keratin), results in abnormal vessels, skin, and hair. Mechanical instability of vessel collagen and remodeling could be mechanisms for the
initiation and development of tortuous blood vessels. Early initiation of copper-histidine therapy may modify disease progression, but prognosis remains poor.

**Author contributions**
L.K.S.: patient management, literature review, and initial draft manuscript preparation. R.S.: patient management, critical review of manuscript for important intellectual content, and final approval of the version to be published. S.V.: analysis of the radiologic data and critical review of manuscript. A.R.: analysis of hair microscopy and critical review of the manuscript. N.S.: clinician in charge, concept and design of the report, critical review of manuscript for important intellectual content, and final approval of the version to be published.

**Study funding**
No targeted funding reported.

**Disclosure**
The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

**References**

**Mystery Case responses**
The Mystery Case series was initiated by the Neurology® Resident & Fellow Section to develop the clinical reasoning skills of trainees. Residency programs, medical student preceptors, and individuals were invited to use this Mystery Case as an educational tool. Responses were solicited through a group email sent to the American Academy of Neurology Consortium of Neurology Residents and Fellows and through social media. We received 148 responses. The majority of respondents (80%) had been in practice for 1–4 years; 68% were residents or fellows, while 20% were faculty/board-certified physicians. A total of 51% resided outside the United States. A wide range of practice settings was represented.

First, respondents were presented with a brief summary of the patient’s presentation (5-month-old boy born to
a consanguineous couple, presenting with drug-refractory seizures and hypotonia on examination) and asked to identify the key findings in figure 1, A and B. Microcephaly was correctly identified by 23% of the respondents, kinky hairs by 60%, loose skin folds by 39%, pili torti (twisted hairs) by 22%, and trichorrhexis nodosa (weak points or nodes causing hair to break off easily) by 9%. The hair abnormality was incorrectly identified as alopecia areata by 29% of the respondents; this term refers to an autoimmune baldness that may sometimes be associated with neuroimmunologic conditions like myasthenia gravis.1

Second, respondents were shown the child’s skeletal X-rays and MRI/magnetic resonance angiography brain (figure 2, A–D), and asked to identify the key findings. Tortuous intracranial arteries were correctly identified by 55% of the respondents, and tortuous extracranial arteries by 28%. The more subtle finding of metaphyseal spurs was accurately identified by 21%, and wormian bone (extra bone within cranial sutures) by 17%. A total of 22% incorrectly identified the patient’s bone abnormality as fibrous dysplasia; this involves replacement of normal bone with large fibrous stroma and islands of immature woven bone and can be seen in disorders like McCune-Albright syndrome (with precocious puberty and café-au-lait spots).2

Finally, when asked to identify the most likely diagnosis (and associated gene) for the patient on the basis of these findings, 72% of the respondents correctly identified this as a case of Menkes disease with ATP7A mutation. The most frequent alternative choice was mucopolysaccharidosis IIIA (5%), a severe early childhood neurologic condition caused by autosomal recessive SGSH mutations. In addition to developmental delay and behavioral problems, these patients can also have seizures as well as hair and skeletal abnormalities, with coarse hair texture, stiff joints, and dense calvaria. Tortuous vessels are not usually described in mucopolysaccharidosis IIIA.3

This Mystery Case provides a succinct overview of key clinical and radiologic findings in Menkes disease.

Aravind Ganesh, MD
Department of Clinical Neurosciences, University of Calgary, Canada; Nuffield Department of Clinical Neurosciences, University of Oxford, UK.

References
Opinion and Special Articles

These articles provide timely opinions about important areas in neurology education and training. Relevant topics include medical student teaching, training requirements, work/life balance, board certification, and directions in education. Seeking the assistance of senior faculty members is often useful. Those interested in writing these manuscripts should contact the Resident & Fellow Section editor before submission to inquire about the interest in specific topics.
Opinion and Special Articles: Challenges and opportunities in defining career identity in academic neurology

David J. Lin, MD, Merit E. Cudkowicz, MD, MSc, and Tracey A. Cho, MD

Neurology® 2018;91:670-672. doi:10.1212/WNL.0000000000006284

There has never been a more exciting time to become a neurologist. As we emerge from training in clinical neurology after 4 or more years of residency and fellowship, many of us are faced with the core challenge of how to define and develop our career identity. That is, how do we continue to take great care of our patients, and now also advance our careers and make contributions to a dynamic field? Here, we focus on developing career identity within academic neurology, noting that careers in private practice neurology and other settings have unique sets of challenges, rewards, and opportunities.

In academic neurology, as in academic medicine, the 3 traditional cornerstones are patient care, education, and research. The canonical academic identities are the physician-scientist, clinician-educator, and “triple threat” (clinician, researcher, and educator). The process of developing career identity in academic neurology has always been challenging, often occurring at a critical period of other life milestones, such as purchasing homes or expanding families. Successfully establishing oneself and finding meaning in one’s work is critical for career satisfaction and preventing burnout.1 Today, given the changing landscape of neurology, the process of developing career identity has unique opportunities and challenges. We highlight these issues and discuss potential solutions that can be instituted at the departmental, organizational, and national levels.

Perhaps the most well-paved career track for academic neurologists is that of the physician-scientist. Milestones for career advancement for physician-scientists are relatively clear—grant funding enables protected time, allowing for productivity in the form of publications, which in turn facilitates local, national, and international recognition. While the milestones are relatively clear, emerging as an independent physician-scientist seems more daunting than ever. Several articles in the last decade have highlighted the obstacles facing physician-scientists, including mounting medical school debt, the long years of training required, the growing complexities of both clinical and research documentation, and historically flat to downtrending NIH paylines.2,3 More can be done by academic departments and organizations to help facilitate dual clinician-research careers. First, during clinical training, despite often being in close geographic proximity to basic and clinical scientists, it is not immediately obvious how to become meaningfully involved in a scientific program. On the other side of the coin, many neuroscientists are hungry for clinical perspectives to inform their ongoing research. Thus, more local initiatives such as speaker series, joint conferences, and social events to encourage dialogue about synergistic goals and complementary skill sets between scientists and clinicians, starting during early career phases, would be helpful.

Second, mentored career transition awards for clinician-scientists such as the NIH K award (K08 or K23) are more difficult to obtain,4 certainly as compared to the early 2000s, which saw a doubling in the NIH budget between 1998 and 2003.5,6 Given the stiff competition for limited funding, successful K awards now seemingly require at the minimum preliminary data equivalent to or resulting in a paper, a dedicated mentor and supportive scientific environment, and clear milestones to scientific independence. To this end, pre-K-award
programs such as the NIH R25 grant and AAN Career Development Awards have been successful in helping to provide protected time to acquire some skills and gather preliminary data. Additional or expanded funding along these lines provided by departments and organizations will be helpful to encourage trainees forming an identity in research. Early seed funding for novel ideas and method development that represent a departure from those of established mentors will help support innovation and new perspectives from emerging clinician-scientists.

The comprehensive clinical translation process, from identification of a question in clinical neurology to hypothesis-driven scientific experiments at the bench to drug and device development and clinical trials in humans, requires expertise spanning innumerable aspects of basic, clinical, and translational science. Institutions and organizations should recognize the current gaps in the clinical translation process and strategically focus funding, starting at the level of trainees, to encourage all types of investigation. More support for young investigators to gain specific expertise in drug and device development as well as clinical trials should be provided as these have not been traditional focus areas for career development grants. This also should include the recognition that industry (e.g., biotechnology, pharmaceutical, and medical device companies) can uniquely contribute to the scientific training of young investigators (i.e., via joint academic–industry fellowship programs). As academic and industry interests align, it will also be beneficial for young clinical investigators to learn to manage potential conflicts of interest.

In contrast to the relatively well-worn path towards becoming a physician-scientist, there is no clear track for aspiring clinician-educators. This is unfortunate because as the diagnostic and therapeutic complexity of clinical neurology continues to increase, the value of effective educators in clinical neurology has never been more apparent. Those interested in medical education in neurology usually dedicate additional time during training to teaching medical students and resident peers. Mentors who have been successful in the area of medical education (i.e., residency program directors or medical student clerkship directors) can provide valuable advice. But after training ends, there are no clear or common mechanisms to help residents and fellows develop medical education careers. At many institutions, there is no dedicated academic advancement track for clinician-educators. On this note, and as a first step, academic departments need to

<table>
<thead>
<tr>
<th>Table</th>
<th>Suggested local and national solutions to promote career development for neurology-trained clinician-scientists, clinician-educators, and academic neurologists</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Academic neurologists</td>
</tr>
<tr>
<td>Local/departmental</td>
<td>Create initiatives during residency such as certificate programs or scholarly pursuits that provide neurology trainees with additional structure and mentorship around specific focus and interest areas (i.e., global health, diversity and inclusion, quality and safety)</td>
</tr>
<tr>
<td>Critically evaluate and learn from programs and structures that help support clinician-scientists and clinical educators</td>
<td>Provide seed funding to develop novel ideas and methods</td>
</tr>
<tr>
<td>Support academic-industry partnerships geared toward development of young clinician-scientists (i.e., joint fellowship programs)</td>
<td>Develop clear milestones for academic advancement of education-oriented faculty</td>
</tr>
<tr>
<td>Organizational/national</td>
<td>Develop support structures for nontraditional academic neurologists; i.e., neurologists focused on hospital medicine (neurohospitalists), patient safety, or global health, among others</td>
</tr>
<tr>
<td></td>
<td>Create formal programs for young investigators to gain expertise in clinical trials and drug and device development</td>
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ACGME = Accreditation Council for Graduate Medical Education.
recognize the unique value that effective clinician-teachers bring to neurology and establish clear milestones for career advancement for education-focused faculty. Different from grants and papers in the research track, such milestones may include patient outcome metrics, teaching awards, or feedback by trainees and peers on teaching and mentorship.

One of the main challenges is funding for careers in neurology education. There are currently no funding mechanisms to support time dedicated to teaching. Here we draw a distinction between developing teaching skills in neurology vs medical education research. To preserve the art of clinical neurology, funding should be dedicated to developing the unique set of skills necessary for highly effective and engaging teaching of clinical neurology. This could come in the form of departmental or national courses and conferences with specific and objective curricula for developing neurologic teaching skills. Accreditation Council for Graduate Medical Education-accredited fellowship programs for neurology educators should be developed. Master Clinician programs within academic departments that bring together education-oriented faculty at all levels could provide (1) real-time patient-focused teaching and feedback on the neurologic history, examination, diagnosis, and management to trainees; (2) a community of faculty with distinct clinical experience and expertise; and (3) synergy and structure around clinical education.

It would be naive and perhaps wishful to think that funding in our current model of reimbursement would provide substantial protected time for young faculty to teach. To this end, creative sources of funding for education should be considered. Could Medicare recognize the unique talent of clinical educators by earmarking teaching funds for individuals or departments? Or could clinician-educators who have a track record of clinical excellence and expertise receive more in reimbursement for dedicating extra time to teaching trainees during a patient encounter?

We have thus far discussed the process of defining career identity for clinician-scientists and clinician-teachers, but what about new and emerging identity templates in academic neurology? For example, the growing volume, demand, and complexity of inpatient neurology services coupled with national pressure to reduce in-hospital length of stay has fueled the birth and growth of the neurohospitalists, who specialize in the high quality and efficient delivery of in-hospital care to neurology patients. How do neurohospitalists create academic identity as they negotiate their funding and time among clinical care, education, and research? Furthermore, patient safety and quality, neurology in the developing world (global health), and diversity and inclusion both in departments and in the field are all critical conversations in neurology today. We need to cultivate residents, fellows, and young faculty with mentorship, protected time, and clear milestoness for career advancement in all of these areas. Initiatives during residency programs such as certificate programs, tracks, or scholarly pursuits that provide additional training, mentoring, and structure can help trainees explore different interests early on. We should evaluate the programs and structures that are working for clinician-scientists and what is starting to work in the area of clinical education for inspiration to help develop experts in neurology quality and safety, global health, and diversity and inclusion.

More can be done at the departmental and national levels to support the academic development of young neurologists. Aspiring clinician-scientists would benefit from additional early-career funding to develop novel ideas and methods as well as more formalized training in clinical trial methodology as well as drug and device development. Clinician-educators would benefit from specific programs focused on the development of clinical teaching skills, finding concrete ways to dedicate funds for time spent on teaching, and the development of clear milestones for academic institutional advancement. Ongoing evaluation of structures and programs for clinician-scientists and clinician-educators will inform the development of other identities in academic neurology (table). Such upfront investments by departments and national organizations will help prevent burnout, maximize career satisfaction, and usher in the next generation of leaders in neurology.

Author contributions
David Lin: manuscript concept, manuscript draft. Tracey Cho: manuscript concept, manuscript draft. Merit Cudko-wicz: manuscript concept, manuscript revision.

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Disclosure
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References
Pearls & Oy-sters

“Pearls and Oy-sters” is a feature focusing on fundamental clinical neurology. Each article addresses a specific niche of neurological disease and provide expertise in the form of clinical insights and tips, i.e., “pearls,” as well as advice for avoiding mistakes, or “oy-sters.” The author may choose to address a particular facet of the approach to neurological disease such as localization, elaboration of a differential diagnosis, evaluation, or treatment. These articles concentrate on what may be found in a textbook and/or provide what textbooks cannot, in the form of knowledge rendered from clinical experience. The target audience consists of those in training; however, the subject matter should be of interest to all in the world of clinical neurology.
Pearls & Oy-sters: Alternating hemiplegia of childhood mimics focal epilepsy and paroxysmal dyskinesia in infancy

Monica B. Dhakar, MD, MS, and Nigel S. Bamford, MD

*Neurology*® 2018;91:47-49. doi:10.1212/WNL.0000000000005745

Pearls

- Paroxysmal dyskinesia is often seen in patients with alternating hemiplegia of childhood (AHC).
- Paroxysmal dyskinesia may be the first presentation of AHC and can precede the hemiplegic attacks by several months.
- These dystonic movements can mimic focal seizures, which are also seen in 40% to 50% of patients with AHC.

Oy-sters

- AHC should be considered in infants presenting with paroxysmal dyskinesia.
- Paroxysmal dyskinesia can often be misdiagnosed as seizures, and some patients may respond to anticonvulsant treatment.
- Video EEG is helpful in distinguishing the underlying diagnosis, particularly in AHC in which seizures and paroxysmal dyskinesias may coexist.

Case report

A 4-month-old boy presented with new-onset paroxysmal spells that began at 10 weeks of age. The initial events consisted of forced head and eye deviation to the left, with a left-beating horizontal nystagmus lasting approximately 5 minutes. He was the product of a full-term pregnancy without complications. He fed well and was achieving all of his early developmental milestones. Family history was unremarkable for neurologic disease. The child’s initial examination revealed mild central hypotonia, but was normal otherwise. A routine sleep-awake EEG was normal but failed to capture an episode. Similar spells occurred weekly, but he had no unusual movements during sleep. During some events, he seemed less interactive with his surroundings and on occasion experienced mild respiratory distress and perioral cyanosis. A presumptive diagnosis of seizures was made, and he was treated with increasing doses of levetiracetam. Despite treatment, the events increased in frequency and duration, some lasting 20 minutes with associated stiffening of either arm, head deviation, and tonic gaze preference. The lack of clinical response to anticonvulsant medication raised the suspicion for nonepileptic attacks (seizure mimics) and he was admitted to the hospital for further evaluation. Brain MRI, serum electrolytes, liver function tests, lactate, plasma amino acids, and urine organic acids were unremarkable. CSF was acellular and revealed normal protein and glucose levels. Neurotransmitter metabolites indicated a slightly low homovanillic acid of 429 nmol/L (range: 450–1,132 nmol/L). 5-Hydroxyindoleacetic acid, 3-O-methyl dopa, neopterin, tetrahydrobiopterin, and 5-methyltetrahydrofolate were normal. Video EEG monitoring captured a paroxysmal event, characterized by head and gaze deviation to the right side, stiffening of the right arm, and poor interaction with his surroundings (video). The event was uninterrupted by physical and verbal stimulation and was terminated by sleep. The EEG
recording revealed normal background for age without any abnormal electrographic changes, consistent with paroxysmal dyskinesia.

The differential diagnosis of paroxysmal dyskinesia during infancy encompasses a variety of genetic and metabolic causes (table). A detailed investigational panel evaluating these etiologies was sent. Genetic analysis demonstrated a de novo heterozygote mutation in ATP1A3, a gene associated with 75% of cases of sporadic AHC, confirming the diagnosis.12 By 8 months of age, the paroxysmal dyskinesias abated and he developed classic attacks of alternating hemiplegia overlaying a baseline global developmental delay. Benzodiazepines and acetazolamide provided some intermittent relief, while oxcarbazepine, topiramate, and flunarizine had little effect. A ketogenic diet was initiated, and at the time of this submission, shows promise in reducing the number of attacks. Follow-up EEG and MRI studies remained normal.

Table Differential diagnosis of paroxysmal dyskinesia in childhood

<table>
<thead>
<tr>
<th>Genetic</th>
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</thead>
<tbody>
<tr>
<td>Dopa-responsive dystonia (GTP cyclohydrolase 1, tyrosine hydroxylase, sepiapterin reductase)</td>
</tr>
<tr>
<td>Alternating hemiplegia of childhood (ATP1A3)</td>
</tr>
<tr>
<td>Paroxysmal kinesigenic dyskinesia (PRRT2)</td>
</tr>
<tr>
<td>Primary paroxysmal nonkinesigenic dyskinesia (mapped to chromosome 2q31-36)</td>
</tr>
<tr>
<td>Paroxysmal exercise-induced dyskinesia (unknown)</td>
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<tr>
<td>Glut-1 transporter (SLC2A1)</td>
</tr>
<tr>
<td>Primary torsion dystonia (DYT1)</td>
</tr>
<tr>
<td>Myoclonus dystonia (SGCE)</td>
</tr>
<tr>
<td>Infantile parkinsonism dystonia (SLC6A3)</td>
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<tr>
<td>Huntington disease</td>
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<tr>
<td>Metabolic disorders</td>
</tr>
<tr>
<td>Glutaric aciduria type 1 (GCDH)</td>
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<tr>
<td>Mitochondrial disease (many)</td>
</tr>
<tr>
<td>Infantile-epileptic dysskinetic encephalopathy (Xp21.3)</td>
</tr>
<tr>
<td>Drugs/toxins</td>
</tr>
<tr>
<td>Hypoxic-ischemic injury, acute or late manifestation of</td>
</tr>
<tr>
<td>Bilirubin deposition in the basal ganglia (kernicterus)</td>
</tr>
<tr>
<td>Copper (Wilson) and iron deposition (PKAN) and others</td>
</tr>
<tr>
<td>Carbamazepine, antihistamines, antipsychotics, antiemetics, and other drugs</td>
</tr>
<tr>
<td>Methanol and carbon monoxide (delayed symptoms are common)</td>
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<tr>
<td>Mimics</td>
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<tr>
<td>Transient paroxysmal dystonia of infancy</td>
</tr>
<tr>
<td>Infantile spasms and focal epilepsy</td>
</tr>
<tr>
<td>Sandider syndrome with gastroesophageal reflux</td>
</tr>
<tr>
<td>Normal (funky) baby movements</td>
</tr>
<tr>
<td>Abbreviation: PKAN = pantothenate kinase-associated neurodegeneration.</td>
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</tbody>
</table>

Discussion

AHC is a rare disorder with an incidence of 1 in 1 million individuals.2 Most cases are sporadic; however, in the rare familial cases, the inheritance is autosomal dominant.3 The most common mutation involves the ATP1A3 gene.1 ATP1A3 is a part of the a subunit of Na+/K+ adenosine triphosphatase (ATPase) protein, which is responsible for normal transport of ions across neuronal membrane. The mutation reduces the activity of Na+/K+ ATPase without affecting the protein levels, resulting in impaired functioning. Mutation in the ATP1A3 gene is also associated with 2 other movement disorders: rapid-onset dystonia-parkinsonism and the syndrome of cerebellar ataxia, areflexia, pes cavus, optic atrophy, and sensorineural hearing loss (CAPOS).4

The spectrum of clinical symptoms of AHC is broad and consists of episodic hemiplegia or quadriplegia, dystonic posturing, choreoathetoid movements, abnormal ocular movements, developmental delay, and progressive cognitive impairment.5 The first attack usually occurs between 3.5 and 7 months of age, although symptoms can be seen as early as the second day of life.5,6 The diagnostic criteria for AHC have been defined below.5 Of these, criteria 1, 2, 3, and 7 are required for a definitive diagnosis of “typical” AHC.

1. Onset of paroxysmal events before 18 months of age
2. Repeated attacks of hemiplegia with attacks on right and left side of the body
3. Episodes of bilateral hemiplegia or quadriplegia starting either as generalization of hemiplegia attack or bilateral from the onset
4. Other paroxysmal events, such as tonic/dystonic attacks, nystagmus, strabismus; dyspnea or autonomic disturbances during the hemiplegia attack or in isolation
5. Disappearance of the symptoms with sleep followed by recurrence upon awakening
6. Evidence of developmental delay, cognitive impairment
7. Not attributable to any other cause

Hemiplegic attacks as the first sign of AHC is seen in only one-third of cases, whereas in the remainder, it is often followed by dystonic episodes or ocular abnormalities such as nystagmus. In fact, the incidence of dystonic episodes preceding the hemiplegic attacks is highest during the first 3 months of life.5 In our patient, the dystonic attacks preceded the hemiplegic attacks by 4 months. He was also noted to have transient abnormal ocular movements. Because of the variability in presenting symptoms, the diagnosis is challenging and can often be delayed or misdiagnosed as epilepsy. Although tonic gaze is a common
presenting symptom of AHC, it is a hallmark of focal seizures and presents a diagnostic challenge that is aided by video EEG. Co-occurrence or late occurrence of epileptic seizures with autonomic features is seen in 40% to 53% of patients with AHC. These patients often have autonomic dysfunction causing flushing, sweating, mydriasis, and sometimes respiratory distress with cyanosis, again mimicking seizures. However, features of bilateral episodic nystagmus or gaze deviation and periods of intermittent and alternating stiffening of extremities lasting minutes to hours with preserved responsiveness differentiate dystonic spells from seizures and should prompt the investigations toward this condition.

Treatment of AHC is challenging. The spells often abate with sleep, and efforts to identify and reduce triggers such as unexpected stimuli and stress are required. Treatment of AHC is symptomatic and is directed toward reducing the severity and duration of the paroxysmal spells. Anticonvulsant and calcium channel blockers are often used with variable success. Alternatively, drugs such as acetazolamide or the ketogenic diet that may modify cellular pH, y-aminobutyric acid, or metabolic pathways have been attempted. Such treatments may modify the neuronal membrane potential or the probability of neurotransmitter release but the mechanism is indirect and their efficacy remains unproven. The severity of the disease appears to be related to the genetic mutation, and whether treatment improves developmental outcome in addition to the frequency of the spells remains unclear.

**Author contributions**

Dr. Monica B. Dhalak: study concept, design, data acquisition, and drafting the manuscript. Dr. Nigel Bamford: study concept, design, intellectual content, and revising the manuscript.

**Study funding**

No targeted funding reported.

**Disclosure**

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

**References**


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Residency Training

These manuscripts will address issues related to residency training, including educational initiatives, programs, opinions, and other topics related to neurology education and training. Relevant topics could include work hours and sleep deprivation, the role of neurocritical care or outpatient neurology in training, quality assurance initiatives, incorporation of evidence-based neurology into training, medical student teaching, work/life balance, and others. Seeking the assistance of senior faculty members is often useful.
Residency Training: The Review Committee for Neurology

Revisions to the Common Program Requirements

Kathryn S. Nevel, MD, Andrew M. Southerland, MD, MSc, Shannon M. Kilgore, MD, and Laurie Gutmann, MD

*Neurolgy* 2018;90:41-44. doi:10.1212/WNL.0000000000004766

As part of a scheduled review of the Common Program Requirements, the Accreditation Council for Graduate Medical Education (ACGME) recently implemented amendments to Section VI, “Resident Duty Hours in the Learning and Working Environment,” which went into effect on July 1, 2017. Prior to July 1, changes to Section VI of the Common Program Requirements were last implemented by the ACGME in 2011. The purpose of this review is to discuss the recent changes to Section VI of the ACGME Common Program Requirements.

**Accreditation Council for Graduate Medical Education**

The ACGME accredits residency and fellowship programs and sponsoring institutions, with dedicated resources to addressing aspects of the clinical learning environment. While the ACGME spearheads many initiatives to enhance the clinical learning environment, the ACGME’s principal mission is to improve health care and population health by assessing and advancing the quality of resident physician education through accreditation. The ACGME oversees 29 Review Committees; each Review Committee accredits all training programs within its respective specialty.

**Review Committee for Neurology**

The Review Committee for Neurology comprises 13 members: 3 organizations each nominate 3 members: the American Board of Psychiatry and Neurology, the American Academy of Neurology (AAN), and the American Medical Association; the Child Neurology Society nominates 1 member; and 1 member represents the American Osteopathic Association. A public member and a resident member are selected by the Committee through an application process. The resident member serves on the Committee for 2 years; the other members serve 6 years each.

The Review Committee for Neurology serves to accredit adult and child neurology residency programs, as well as fellowship programs in 9 subspecialties. Programs are accredited through review of annual Resident and Faculty Survey results, board pass rates, educational curriculum, faculty and resident scholarly activity, and site visit information. The Common Program Requirements, defined by the ACGME, cover a broad range of topics in the clinical learning environment regardless of specialty and include requirements for institutional and program resources, resident appointments, evaluations, patient safety, work hour limits, professionalism, transitions of care, and supervision. Educational curriculum and clinical requirements are determined by each specialty Review Committee; the Review Committee for Neurology completes neurology-specific requirements.

**Duty hour regulations**

Resident duty hour regulations attempt to balance 2 competing aims: the safety of residents’ current patients and that of their future patients through residents’ attainment of medical knowledge and skills. Ensuring this delicate balance is challenging and requires ongoing assessment of both patient and physician outcomes.
In 2003, the ACGME adopted the following duty hour regulations into the Common Program Requirements: a maximum 80-hour work week, 1 day off in 7 averaged over 4 weeks, and maximum 24 hours of scheduled continuous duty with up to 6 additional hours allowed. In 2009, the ACGME commissioned a task force to review the duty hour standards implemented in 2003. Due to testimony and literature indicating interns worked longer hours than senior residents, and that more errors occurred from fatigue, the ACGME added more requirements in 2011. These requirements include that interns cannot exceed 16 hours of continuous work, upper level residents cannot exceed 24 hours of continuous work plus an additional 4 hours allowed for specific circumstances, residents must have 14 hours off between 24-hour shifts and 8 hours off between other shifts, and night duty is limited to 6 consecutive nights.

Though the 2011 standards were adopted, the medical community debated their benefit to patient care, resident education, and resident well-being. In January 2016, the AAN, along with more than 60 other member organizations, submitted a position statement to the ACGME describing unintended consequences of the current duty hour restrictions. Though intern work hours are not typically directed by neurology programs, the AAN expressed concern that limiting intern work hours left residents unprepared for the longer hours and greater patient responsibilities of PGY-2 years. Other unintended consequences of the current duty hour regulations include decreased continuity of care, increase in patient handoffs, and increase in shift work mentality.

The only prospective study on duty hour regulations among neurology residency programs evaluated residents on measures of burnout, sleepiness, and satisfaction with patient care and education, as well as faculty satisfaction with resident patient care and knowledge. The study used a control month using the 2003 ACGME duty hour requirements, and an intervention month using more restrictive requirements limiting the number of continuous hours worked. During the intervention month, residents reported lower scores in quality of life, patient care, and satisfaction with education, while faculty reported lower scores on resident knowledge and quality of care. There was no improvement in resident sleepiness or increase of sleep time during the intervention month, despite the shorter shift length. Though small, this study suggested more restrictive work hours during training may adversely affect neurology resident education and patient care.

In more recent years, 2 additional prospective trials have evaluated the effect of longer continuous work hours on resident and patient outcomes. The Flexibility in Duty Hour Requirements for Surgical Trainees (FIRST) trial is a national randomized trial among general surgery residents comparing the 2011 duty hour regulations to a more flexible schedule, allowing residents to work longer continuous hours. Results from the 2014 to 2015 years revealed non-inferiority in the flexible group on almost all patient outcome measures; residents in the flexible group were less dissatisfied on metrics of perceived quality of patient care and trainee education, but more dissatisfied on some individual measures of personal well-being. The trial was extended to the 2016–2017 years, with results pending. A similar trial, Individualized Comparative Effectiveness of Models Optimizing Patient Safety and Resident Education (iCOMPARE), among internal medicine programs completed participation in July 2016, with results pending. Characteristics and outcomes of these 3 prospective duty hour studies are summarized in table 1.

Section VI of the Common Program Requirements: Changes

In late 2015, the ACGME scheduled a revision of the entire Common Program Requirements. A task force comprising members of the ACGME Board of Directors, along with Chairs and resident members of various Review Committees, was formed to revise Section VI of the Common Program Requirements: "Resident Duty Hours in the Learning and Working Environment." Revision of Sections I–V is still in process. This task force reviewed scientific literature, position statements from medical member organizations, comments from the public sector, and testimony at the ACGME Congress in March 2016 before rewriting Section VI. Proposed modifications were published on November 4, 2016, followed by a 45-day public comment period. The task force reviewed all comments before submitting a revised Section VI to the ACGME Board of Directors. The Board approved the finalized version, which was announced at the ACGME Educational Conference on March 10, 2017, and were implemented across all ACGME-accredited training programs on July 1, 2017. Though many changes were made to Section VI, work hour regulation modifications will serve as the most visible difference in residency training.

Duty hours, renamed “Clinical Experience and Education” in Section VI, includes several notable modifications, listed in table 2. The new regulations extend continuous hours worked for interns to 24 hours, and allow trainees to continue working beyond the maximum 24 continuous hours scheduled, if on their own initiative. Clinical work conducted from home must now be counted toward the unchanged maximum 80-hour work week. Additional changes detail aspects of a supportive and effective clinical learning environment, and include modifications to address patient safety, quality improvement, supervision, and accountability, and add requirements to support physician well-being.

By allowing flexibility within programs to create schedules that best support their clinical learning environment, it is anticipated that patient safety and trainee education will be enhanced. Extending interns’ continuous work hours will allow interns to function as equal partners on the team, improving continuity of care as well as education. It will also minimize delay in resident maturation during intern year, particularly important to neurology programs, since PGY-2 residents are often on the frontlines in their new specialty. As neurology residents continue clinical work from home in the form of...
<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Trainee outcomes</th>
<th>Other outcomes</th>
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<tr>
<td>FIRSTa</td>
<td><strong>Participants</strong>&lt;br&gt;PGY-1–PGY-5 Surgery residents (4,330 residents from 117 programs)</td>
<td><strong>Primary</strong>:&lt;br&gt;No significant difference in resident dissatisfaction with overall education or well-being</td>
<td><strong>Primary</strong>:&lt;br&gt;Noninferiority of flexible group for death and serious complications</td>
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<td><strong>Study design</strong>&lt;br&gt;Programs randomized to “standard-policy” group (2011 requirements) vs “flexible-policy” group (intervention)</td>
<td><strong>Secondary</strong>:&lt;br&gt;Flexible group less likely to perceive a negative effect of duty hours on patient care; flexible group more likely to perceive negative effect on various measures of personal well-being</td>
<td><strong>Secondary</strong>:&lt;br&gt;Noninferiority of flexible group for any complication, unplanned reoperation, or infection; inconclusive for unadjusted 30-day mortality, though flexible group noninferior in the adjusted analysis</td>
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<td><strong>Intervention</strong>&lt;br&gt;PGY-1 residents can work &gt;16 hours; PGY-2–PGY-5 residents can work &gt;24 hours; no amount of required time off between shifts for any PGY level</td>
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<td>iCOMPAREb</td>
<td><strong>Participants</strong>&lt;br&gt;PGY-1–PGY-3 Internal medicine residents (63 internal medicine residency programs)</td>
<td><strong>Ongoing</strong>, results not published; assessing trainee sleep duration, behavioral alertness, self-perceived sleepiness, time spent in direct patient care, trainee satisfaction with education</td>
<td><strong>Ongoing</strong>, results not published; assessing patient 30-day mortality rate, rate of prolonged length of stay, total costs of patient care</td>
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<td><strong>Study design</strong>&lt;br&gt;Programs randomized to “standard-policy” group (2011 requirements) vs “flexible-policy” group (intervention)</td>
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<td><strong>Intervention</strong>&lt;br&gt;Flexible schedules determined by programs, but must comply with 80-hour work week, call no more than every 3 days, 1 day off in 7 (all averaged over 4 weeks)</td>
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<td>Neuro IOMc</td>
<td><strong>Participants</strong>&lt;br&gt;PGY-2–PGY-4 Neurology residents (34 residents from 3 residency programs)</td>
<td><strong>Residents</strong> reported greater dissatisfaction with quality of life at work, knowledge of patients, and continuity of care, and increased burnout during the flexible month; no difference between control and intervention months on measures of time spent on educational activities or sleep</td>
<td><strong>Attending physicians more dissatisfied with residents' knowledge and quality and continuity of care of patients, as well as preparedness for rounds</strong></td>
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<td><strong>Study design</strong>&lt;br&gt;Each participant spent 1 month in control group with 2003 requirements allowing “24 + 6” hours on duty, and 1 month in the intervention group</td>
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<td><strong>Intervention</strong>&lt;br&gt;Residents limited to shifts of 16 continuous hours (or 24 hours with 5-hour nap); no averaging of call shifts; maximum of 4 consecutive nights</td>
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a Flexibility in duty hour requirements for surgical trainees, data from 2014 to 2015 academic year, results from 2015 to 2017 pending.8
b Individualized comparative effectiveness of models optimizing patient outcome and resident education, enrollment began 2015, with results pending.9
c Neurology prospective duty hour study, 2011.7
Table 2 Highlighted changes in Section VI of the Common Program Requirements\(^a\)

| PGY-1 residents may work 24 continuous hours, allowing 4 additional hours for certain circumstances |
| Residents may stay beyond the traditional "24 + 4" hours on their own initiative, for educational or clinical continuity purposes, and return to the hospital with fewer than 8 hours off |
| Night float may be scheduled for more than 6 consecutive nights (must adhere to 1 day off in 7, averaged over 4 weeks) |
| Clinical work performed from home must be counted into the 80-hour work week maximum (averaged over 4 weeks) |

\(^a\) Changes effective July 1, 2017: Clinical Experience and Education Regulations.

patient documentation and after-hours patient and hospital calls, the incorporation of work performed from home into the 80-hour work week will require careful attention to ensure residents do not exceed the 80-hour maximum. Both positive and negative outcomes resulting from these changes will be monitored by the Review Committee for Neurology through standard ACGME monitoring processes, including the Resident and Faculty Surveys and site visits.

Conclusion
Clinical experience and education work hour regulations influence resident and fellow education, patient safety, and physician well-being. Prospective studies suggest that shorter continuous work hours lead to a decrease in both educational and clinical outcomes without improvement in patient care. The new requirements in the Common Program Requirements lessen restrictions on work hours, allowing programs flexibility to individualize schedules to best fit program needs. Section VI of the ACGME Common Program Requirements will require continued reassessment to ensure the safety of today’s and tomorrow’s patients in a supportive clinical learning environment.

More information can be found at www.acgme.org.

Author contributions
Kathryn Nevel: acquisition of information, drafting and revising the manuscript. Andrew Southerland: drafting and revising the manuscript. Shannon Kilgore: drafting and revising the manuscript. Laurie Gutmann: drafting and revising the manuscript.

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References
Right Brain

Right Brain is a feature devoted to the relationship between neurology and the medical humanities, with submissions either written by trainees or with a focus on the experience of the trainee. Appropriate submissions include articles, commentaries, and reflections on the interaction between neurology and history, literature, ethics, theology, sociology, anthropology, philosophy, poetry, theater, film, fine arts, or the media. Right Brain also will publish original works of fiction, poetry, and reflection written by residents and fellows relating to the practice of neurology or neurology training.
Right Brain: Withholding treatment from a child with an epileptic encephalomyopathy

Aaron Rothstein, MD, and Ariane Lewis, MD

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Abstract

The case of Charlie Gard, an infant who was hospitalized in England due to a mitochondrial DNA depletion syndrome that led to an epileptic encephalomyopathy, was highly publicized. Though Charlie’s parents lobbied for him to receive experimental nucleoside replacement therapy as a desperate effort to save him, this request was denied, and after a lengthy legal battle, he died in late July 2017. We discuss the ethical considerations and consequences of this case.

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Mitochondrial DNA depletion syndromes are autosomal recessive oxidative phosphorylation disorders characterized by a reduction in mitochondrial DNA leading to severe clinical symptoms. Charlie Gard, an infant with a mitochondrial DNA depletion syndrome, died from an incurable epileptic encephalomyopathy (a disorder characterized by seizures, altered mental status, and weakness) in a hospital in England in July 2017. His story was highly publicized and imbued with controversy as his family sought to treat him with experimental nucleoside replacement therapy. Herein, we discuss the ethical considerations and consequences of this case.

Case report

In August 2016, Charlie was born at Great Ormond Street Hospital (GOSH) in England. When he was 8 weeks old, he became weak and began to lose weight. Testing revealed that he had a mutation in the RRM2B gene, which encodes the ribonucleotide reductase M2B subunit protein, resulting in the depletion of mitochondrial DNA. He subsequently developed respiratory failure requiring a ventilator, tetraplegia (with only occasional eye opening), and epilepsy. His parents were told that this syndrome would result in death in months. Charlie’s parents found neurologists in both Italy and the United States willing to give him an experimental nucleoside replacement therapy, a treatment that has only been used in patients with myopathy due to a different mitochondrial DNA depletion syndrome. However, because of the severity of Charlie’s epileptic encephalomyopathy, GOSH did not allow him to receive the therapy or be transferred. GOSH petitioned the High Court in Britain for permission to take Charlie off the ventilator and focus on comfort measures only. The Court granted this request. Charlie’s parents appealed the decision, but multiple British courts denied their appeal. Charlie’s case captured the attention of the world, resulting in public comments from the Pope and President Trump and an international petition with 350,000 signatures supporting Charlie’s parents’ pleas for the right to administer the experimental nucleoside replacement therapy. In the midst of a protracted 6 months of court proceedings and ethical debate, Charlie deteriorated. In July 2017, his parents acquiesced that the situation was hopeless and that it was too late to help him. He was transferred to hospice, care was withdrawn, and he died.

Discussion

Should Charlie have been given experimental therapy? From his parents’ perspective, this therapy was the only way to prolong their son’s life. But did they understand that data for the therapy were limited? Were their expectations realistic or overly optimistic? Were they focused on Charlie’s best interests, or were they motivated by grief? From the hospital’s perspective, Charlie’s disease was very severe, the therapy was unproven, and it may have protracted his suffering. But was it appropriate for them to prevent other physicians from giving him the therapy? In order to determine whether or not Charlie should have been given the experimental therapy, we must consider the basic ethical principles of beneficence, nonmaleficence, and autonomy.

Was there potential for nucleoside replacement therapy to be beneficent (beneficial) to Charlie? Because nucleoside replacement therapy has never been used for RRM2B mitochondrial DNA depletion syndrome, we have no way of knowing if he would have benefited from this therapy. Nevertheless, limited data suggest that it was effective for another mitochondrial DNA depletion syndrome, a TK2 mutation—it led to improved muscle strength and head support in a 3-year-old child and significantly prolonged the lifespan of mice with this disorder. But a TK2 mutation only leads to a myopathy, not an epileptic encephalomyopathy, so would this therapy have helped a patient with a RRM2B mutation? Given that it is unclear if this experimental therapy would have been efficacious in this setting, its administration would have been considered compassionate use.

Even if the therapy prolonged Charlie’s life, would it have violated the principle of nonmaleficence by causing harm or extending his suffering? Although the therapy has only been used in a limited number of cases of TK2 mutations, it is not known to cause any serious adverse effects. Thus, assessing whether the therapy would cause harm relied largely on a determination of whether or not Charlie was suffering. Notably, attempts to prolong life despite the possibility of causing discomfort are often made for patients with terminal diseases such as metastatic cancer, but these decisions are generally made by patients themselves. Because Charlie was a minor and had no ability to communicate, surrogates, including his parents, the hospital, and the courts, had to make decisions on his behalf. Determining whether he was suffering must have been challenging given that he was tetraplegic, nonverbal, and only occasionally opened his eyes. Surely, parents would not want to prolong their child’s suffering, so his parents must not have thought he was uncomfortable. GOSH, however, must have believed otherwise.

If GOSH did not think it was appropriate to give Charlie this therapy, he could have received it if he was transferred to New York or Italy. A decision of whether or not to transfer him should not have been based on the hospital’s assessment of
whether the therapy itself could help or harm him, but rather on Charlie’s parents’ rights to make autonomous decisions on their child’s behalf and whether the transfer itself would be nonmaleficent. This bears similarities to the well-known case of Baby Joseph, a 13-month-old who had another mitochondrial disorder, Leigh disease, and was in a vegetative state in a hospital in Canada. A Canadian court ruled that, despite his family’s protestations, the hospital could terminally extubate him. Though they understood that Baby Joseph was terminally ill, his family wanted him to be able to die at home. After obtaining support from an organization called Priests for Life, they brought him to the United States, where a tracheostomy was performed. Baby Joseph died at home 6 months later. Baby Joseph’s case clearly established precedence for international transportation despite physician declaration of futility. Transporting patients on ventilators is fairly common, and if a patient is hemodynamically stable and trained medical staff with necessary equipment is present, this process is relatively benign—even across international borders, as the case of Baby Joseph indicates—so it is unlikely that the risks of transfer would have been greater than the potential benefits. Thus, even if GOSH did not believe it was appropriate to administer the experimental therapy, it does not seem to be just of them to deny Charlie the opportunity to receive the therapy elsewhere, as this violated the ethical principle of patient autonomy.

Charlie Gard’s situation was tragic, and it illustrates how challenging it can be to weigh ethical principles, particularly at the end of life. The reality is that Charlie likely would have died with or without experimental nucleoside treatment. However, his parents wanted him to receive this therapy and there were 2 hospitals willing to give it to him. Administering the therapy or transferring Charlie to another hospital willing to give it to him would have been reasonable, practical, and ethically appropriate. While it is unknown whether Charlie was suffering or if the therapy would have been beneficial, the limited available data suggest that it would not have led to serious adverse effects, thereby adhering to the ethical principle of nonmaleficence while striving for beneficence. In addition, allowing Charlie’s parents to make medical decisions on his behalf would have demonstrated respect for their autonomy.

Like the case of Baby Joseph, the case of Charlie Gard will have a long-lasting impact and will be referenced in medical-ethical condemnations in the future. The consequences of the courts’ decisions to deny Charlie the opportunity to be treated with experimental therapy are not restricted to his case. In fact, Charlie’s case was cited in another case in July 2017, when a High Court judge in England ruled that care should be withdrawn from another child with brain damage because of the belief that the child was suffering and was going to die soon anyway. It defies the basic ethical principal of autonomy for physicians and courts to be allowed to unilaterally withdraw care over a patient or family’s objections in cases of perceived medical futility in a setting other than brain death, especially when there is a nonmaleficent and possibly beneficent option available. Interestingly, the importance of patient and surrogate autonomy has previously been noted to be valued more in the United States than in England, so if Charlie had been hospitalized in the United States, we suspect he would have been treated with the experimental therapy.

Neurologists, who often deal with severe, incurable debilitating illnesses, should be skilled at considering their ethical obligations in this type of complex case. Goals-of-care discussions and review of treatment options should always include an honest disclosure of potential risks and benefits and a realistic presentation of the expected outcome. In cases of physician–patient/family disagreement, external assistance should be sought from another clinician or an ethics committee.

Author contributions
Aaron Rothstein was responsible for drafting the manuscript and final approval of the manuscript. Ariane Lewis was responsible for conception, critical revisions, final approval of the manuscript, and supervision.

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All details of this case were extracted from the lay press. The authors had no contact with the patient, his family, or his physicians.

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References
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Teaching NeuroImages: A cutaneous vascular malformation hides giant cerebral aneurysms

Valerio Brunetti, MD, Michela Ada Noris Ferilli, MD, Roberta Morosetti, MD, and Giacomo Della Marca, MD, PhD

Neurology® 2018;90:e1362-e1363. doi:10.1212/WNL.0000000000005304

Figure 1 Brain diffusion-weighted MRI and angio-CT scan

(A) Diffusion-weighted MRI, in the axial plane, shows a hyperintense lesion in the left occipital lobe (acute ischemic stroke). (B) Angio-CT scan (sagittal view). A giant aneurysm (35 × 45 mm) of the left vertebral artery is visible, largely thrombosed. A giant aneurysm (22 × 30 mm) is also present in the left internal carotid artery. White arrows indicate the aneurysmic lesions in the carotid and in the vertebral arteries and the abnormal dilation at the origin of the subclavian artery. Dotted line: profile of the aneurysm of the vertebral artery.

Figure 2 Cutaneous hemangioma

A large hemangioma is visible on the left side of the neck on the cutaneous surface corresponding to the internal arterial malformation.

A 64-year-old man acutely developed right hemianopsia. Brain MRI showed an ischemic stroke in the left occipital lobe (figure 1A). Angio-CT revealed giant aneurysms of the left vertebral and internal carotid arteries (figure 1B); the left subclavian artery and the left jugular vein presented abnormal dilation. On the same side of the neck, he presented a cutaneous lesion

From the Stroke Unit, Institute of Neurology, Catholic University, Rome, Italy.

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consistent with hemangioma (figure 2). The stroke was most likely due to embolization from the vertebral aneurysm.

Cutaneous vascular malformations in the face or neck areas can be associated with cerebrovascular malformations and should prompt an evaluation of the cerebral circulation.\textsuperscript{1,2}

Author contributions
Dr. Brunetti: study concept and design, drafting the manuscript, accepts responsibility for conduct of research, acquisition of data. Drs. Ferilli and Morosetti: analysis or interpretation of data, accepts responsibility for conduct of research, acquisition of data. Dr. Della Marca: interpretation of data, accepts responsibility for conduct of research, study supervision, revising the manuscript, final approval.

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Teaching Video NeuroImages: The signs of dystonic tremor

Tremulous “escanciador”

Jennifer Sharma, MD,* Daniel Macias-Garcia, MD,* Amir Zaidi, MD, and Alberto J. Espay, MD, MSc

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Figure Position of the arm required to elicit the hand tremor

A 58-year-old woman noticed right-hand jerky tremor exclusively while curling her hair. Her tremor-generating posture was reminiscent of the Asturian pourer of cider, or “escanciador,” who holds the bottle above the head when vertically pouring to aerate the liquid (figure). On examination, we asked her to hold a water bottle as if it were a hair curler. This elicited an action-induced, position-dependent, task-specific, weight-sensitive tremor, which attenuated when touching her affected hand with the unaffected one (closed-loop sensory feedback or sensory trick) (video 1). The rest of the examination was normal. These 5 clinical features distinguish dystonic tremor from all other tremor syndromes.1,2

*These authors are neurology residents and contributed equally to this work.

From the Department of Neurology (J.S.), Kingston General Hospital, Canada; Department of Neurology (D.M.-G.), Hospital Universitario Virgen del Rocio, Seville, Spain; and UC Gardner Neuroscience Institute and Gardner Family Center for Parkinson’s Disease and Movement Disorders (A.Z., A.J.E.), Department of Neurology, University of Cincinnati, OH.

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Author contributions
Drs. Sharma and Macias-Garcia drafted the manuscript and videotape. Dr. Zaidi contributed to data acquisition and review of the manuscript. Dr. Espay examined the patient and provided critical review of the manuscript.

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